

THE CASE FOR NEUROFEEDBACK

Clinical Studies and Medical Research

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AN EVALUATION OF DIGITISED NEUROFEEDBACK THE FUTURE OF PERSONALISED MENTAL HEALTH CARE?



October 2021

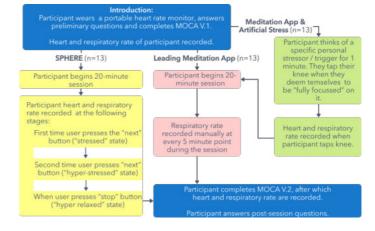
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Background and aims

Neurofeedback is a method of brain self-control via measurement of brainwaves and provision of a feedback signal. Previous literature has identified potential for neurofeedback as alternative treatment for neuropsychiatric conditions including stress and anxiety. The SPHERE tool aims to digitise neurofeedback for mobile devices. This study evaluated whether SPHERE was more effective in improving the common symptoms of stress and anxiety than the most popular alternative digital tool available.

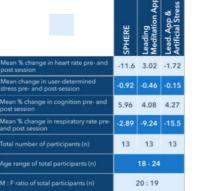
Methods

39 participants were recruited opportunistically. Participants were randomly assigned to 3 groups to test either SPHERE, the widest-used digital tool or the widest-used digital tool with a presession artificial stressor applied. Participant heart rate was recorded preand post-session. 1-tailed Mann-Whitney U Tests or Welch's tests were used to assess significance between cohorts with p<0.05 denoting significance throughout.

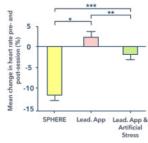


Results

A significantly larger decrease in heart rate pre- and post-session was observed mongst the SPHERE cohort compared to both other cohorts: 11.6% decrease for SPHERE, 3.02% increase for the widest-used digital tool and 1.72% decrease for the widest-used digital tool with a pre-session artificial stressor applied (p < 0.01).







Conclusions

SPHERE's digitised neurofeedback tool was significantly more effective in improving symptoms of stress and anxiety compared to the widest-used alternative digital health tool ± pre-session artificial stressor applied, indicating the benefits of accessible neurofeedback therapy.

More investment is necessary in comparing digital therapies to pharmaceutical treatments for stress and anxiety and for exploration of net changes in brain frequency pre- to post-session to enhance the effectiveness of this tool.

Presented at:



10th European Conference on Mental Health



Imperial College London



WCN 2021 XXV WORLD CONGRESS OF NEUROLOGY ROME, OCTOBER 3-7, 2021

Stress Point Health: Research Protocol Results and Data Analysis 2019



Introduction

Over the last 30 years, stress-related illnesses (anxiety, phobias, PTSD, etc) have become epidemic throughout the developed world which the medical establishment has been slow to address.

While a plethora of tools have existed for decades (and in some cases centuries), the modern focus has been centered around the two mainstays:

drug therapies

"talk-therapies" such as cognitive behavioural therapy (CBT, a specialised way of addressing psychiatric ills).

While CBT and pharmaceuticals have been effective therapies for a specific population of people, in reality, a huge population has been left without effective treatment for these challenging medical issues. In particular, the lack of effective tools to treat stress-related illnesses has fuelled a drug epidemic, an obesity epidemic and substantial diminishment in productivity and performance as patients have tried to self-medicate and struggle to find good solutions to their problems.

We aim to tackle these issues by bringing to a broad cross section of people, a concept which has been established in highly specialised settings for over 30 years. NeuroAcoustic Feedback (NAF) is a unique and profoundly underutilised tool to treat the entire spectrum of stress-related illnesses ranging from mild phobias to complex PTSD and Generalized Anxiety Disorder (GAD). As opposed to using drugs and "talk-therapies," NAF uses soundwaves.

NAF is utilised to harmonise soundwaves to the brain wave activity already constantly present in our brains. By using proprietary algorithms to deliver a personalised sound pattern to a patient, we can "calm the brain" resulting in positive brain wave generation. Specifically, NAF has been shown to increase alpha and theta wave activity in the brain. These waves are strongly associated with restfulness, healing, calming and even euphoria. NAF is quite different from meditation therapies, deep breathing strategies and mindfulness training. All of these modalities require a patient to learn techniques to actively control their anxiety, which is their inherent flaw.

These modalities, much like pharmaceuticals and CBT, are effective, but, only in a small subset of the population, and, in particular, the most severe cases are virtually un-addressable. With NAF, a patient is not forced to actively control their breathing or their thought patterns. Rather, the synchronisation of the soundwave patterns to an individual's unique brainwaves (finding the "Stress Point") organically creates a state of calm and turns negative imagery and feelings into positive imagery.

Historically, NAF was performed by a small group of specialised therapists throughout the world. These treatments were always used at a clinician's office and over a period of weeks in scheduled appointments. Existing equipment is quite clunky, expensive, very difficult to use and was only validated for chronic use. In addition, sessions were expensive and dependent on a therapist being geographically convenient for a patient to be able to access treatment. Although the clinical data was strong, these failures led to minimal adoption of this therapy on a widescale.

With our proprietary processes of automation and guidance (via visual and verbal cueing), the clinical professional has been removed from the treatment.

Additionally, by creating a Smartphone based NAF application, we are able to allow sufferers to safely self-treat virtually anytime and anywhere opening up the option for acute treatments (i.e. to break a panic attack or reduce performance anxiety).

By eliminating the need to see a psychiatric professional, reducing the reliance on medications and the need to be able to control your own anxiety, all the major hurdles to access robust psychiatric care have been eliminated, creating a highly accessible and efficacious treatment for anyone with a smartphone.

Research into Efficacy: Clinical Beta Test

On the 7th, 8th and 9th of August 2019, we conducted a research protocol using our fully functional beta application with 22 unpaid volunteers.

These patients came from the existing patient base of Dr. Michael Bott, a renowned British psychiatrist who has been treating refractory and challenging cases for decades. Additionally, we met and treated a second group of individuals who were introduced to us by a homelessness charity. Whilst our population spanned the whole spectrum of stress-related illnesses, the group was skewed towards the more severe end of the spectrum - the most challenging cases. Many had tried most of the existing treatments available (medication, CBT, mediation apps etc), with little or no success in the long term.

Each volunteer underwent a uniquely individualised 20-minute treatment session performed according to WHO research standards. Throughout the treatment, vital signs (such as heart rate, blood pressure and breathing rate) were monitored both for safety and to identify effectiveness. Although health professionals were in the room monitoring the volunteer, the actual treatment did not require significant interaction with any research staff (it was self-treatment).

Results at a glance

86%

of participants felt an improvement in their Global Impression of Change after the session

50% of the above felt "very much improved" the highest rating

they could give

73%

of participations showed a drop on the anxiety scale between the start and end of the session

95%

showed a drop on the anxiety scale between their Stress Point and the end of the session

86%

showed a drop of 4 or more on the anxiety scale between their Stress Point and the end of the session

"I felt like I wanted to achieve

41%

"Powerful experience"

felt no anxiety at all by the end of the session

something with my day" "My fear turned into excitement" "I was so relaxed by the end"

"I felt like I could sleep for the first time in years"

"I felt a sense of Euphoria"

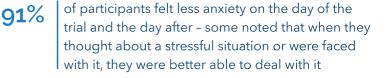
"I felt positive "

"Slept peacefully all night which never happens"

"New view on life"

Follow up stats

- **100%** of participants said they would like to use our technology again
 - 94% of participants asked said they would pay for another session, the remaining 6% didn't know
 - 91% of participants had much improved sleep the day of the trial and the day after, this was especially significant as 100% of participants noted lack of good sleep as one of their symptoms





participants had much improved energy levels the 78% day after the trial

82% of participants felt they were better able to deal with stressful situations following the trial





Anxiety Scales

At various points during the session we asked participants to rate their anxiety levels on a scale of zero to ten. Zero representing a feeling of total calm with no anxiety and ten representing the worst anxiety they have ever felt. The graph below shows the average starting anxiety level and the change throughout the session. To achieve such acute results has a profound impact for users.

Respiratory Rate

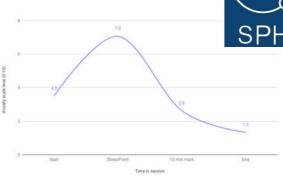
Figure 2 plots the respiratory rate change over the course of the session, measured in breaths per minute.

Long term meditators can see a 1.7 bpm reduction over time - so if we take the high point of people's bpm in our sample you can see that SPH's technology has a far greater impact on bpm, even with only one session. To see a reduction of 1.7 bpm through meditation requires a long-term practice and mastering of meditation techniques.

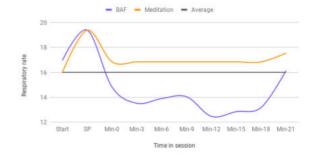


PGIC is a widely used instrument to measure the general effects of a therapeutic measure, particularly with subjective outcomes such as anxiety and pain. PGIC is considered an amalgamated response. Likely, when we asked this question, subjects took into consideration their mood, sense of general well-being, energy level, pain and anxiety, to answer the question posed. In free-form discussion post-treatment, all of these positive effects were noted.

With the knowledge we now have of the wide-ranging positive benefits of NAF, future studies can be performed to assess for specific changes in mood, energy, pain and general sense of well-being. Simply put, this tool is a validated measure of likeability, likelihood to "do it again," and even likelihood to refer. With our pilot, we achieved zero negative ratings suggesting that all our volunteers would at a at minimum try the treatment again and, at best, gave NAF rave reviews.









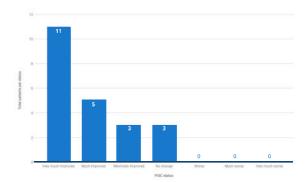


Fig. 3. Patient Global Impression of Change (PGIC)

Conclusion

As you can see from the graphs, the data was quite astounding, far exceeding our most optimistic expectations. Of particular note, is that these results were achieved over one single session of treatment, not a battery of weeks of therapy.

Public Beta Testing - January 2020

Following the success of the first round of research we launched our beta version to the public. Users were able to access two free sessions, 7 days apart through their smartphone. Users recorded their symptoms, anxiety levels before, during and after the session and additional feedback on their experience entirely through the apps' functionality.

Over a period of 3 months we recorded the following results:

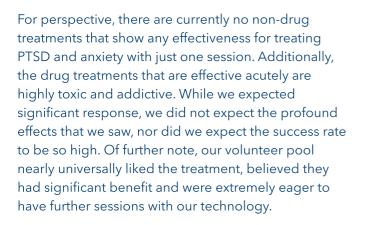


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Summary



Our preliminary data shows acute effectiveness (even in next day follow-up) after just one session. Existing research with NAF has not focused on acute effectiveness. The single session efficacy of App-based NAF is revolutionary. Our early research shows a clear path for taking this treatment out of the doctor's office and into your pocket or purse.



We have also developed a fully automated process eliminating the need to present to a doctor and removing any societal stigmas.

We have additionally identified more robust clinical goals and research options. In partnership with a major academic institution, we aim to validate these results and expand upon them using a much larger patient population. Expansion to show efficacy in other over-lapping but separate illnesses is also planned such as ADHD. NAF's efficacy must be studied in eating disorders, addictions and performance improvement. All these issues have similar alterations in brain wave function which likely can be treated very effectively and very safely with NAF thus expanding the patient base who would benefit from NAF.

In short, the utility of NAF lies in the fact that it can be used acutely and over a period of time from the comfort (and privacy) of your own home without the need for medical professionals or dangerous and potentially addictive medications for a large spectrum of stress-related illnesses and a plethora of similar syndromes.



RESEARCH IN PARTNERSHIP WITH IMPERIAL COLLEGE LONDON

identifying further applications of Stress Point Health's digitised Neurofeedback technology

THE DELIVERY ROOM: THE IMPACT OF OBSTETRIC EVENTS ON THE RISK OF DEVELOPING PTSD POSTPARTUM. A SYSTEMATIC REVIEW

June 2022

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Background and aims

The research aims to determine whether obstetric events impact women's risk of developing PTSD following labour; to evaluate the impact of different types of obstetric events based on the biopsychosocial model (⁵) on women's risk of developing PTSD following labour; and to explore what further research could be conducted to reduce a woman's risk of developing PTSD following labour.

- Roughly 4% of women are left traumatised by their birthing experience. (1)
- 30,000 women in the UK develop postpartum post-traumatic stress disorder (PTSD) annually. (2)
- A survey by the Birth Trauma Association (BTA) found 60% of participants did not know that childbirth could result in PTSD. (²)
- Definition of birth trauma from the BTA: "post-traumatic stress disorder after childbirth." (3)

Classification of PTSD:

- DSM-IV: listed PTSD as an anxiety disorder;
- DSM-V: lists PTSD as a trauma- and stressorrelated disorder. (⁴)

Four categories of symptoms for PTSD according to DSM-V (⁴):

- 1. Re-experiencing;
- 2. Avoidance;
- 3. Negative cognitions and mood;
- 4. Arousal.

Birth Trauma is a major public health issue - research continues to take place to ensure that the physical and mental health of women is looked after postpartum.

Methodology

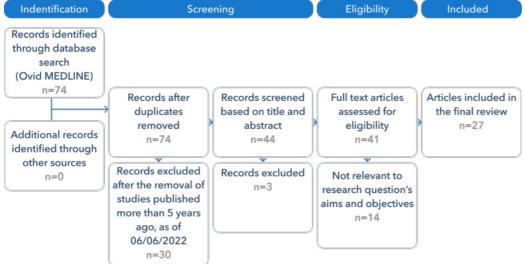


Figure 1: PRISMA flow diagram

Inclusion Criteria	Exclusion Criteria
• Population: people in delivery room at time of parturition.	 Women with a history of PTSD;
 Context: postpartum PTSD. 	• Studies focused on events occurring outside the delivery
• Study design: any.	room;
 Date of publication: 2017- 2022. 	• Studies not available in English.
• Country: global.	

Figure 2: Table showing inclusion and exclusion criteria for studies



1) Definitions:

Obstetric Events: events pertaining to labour that occur in the delivery room, including but not exclusive to: support from birthing partner, healthcare provider communication, subjective pain appraisal, pain relief, type of delivery, obstetric violence (also known as incorrect or inappropriate treatment) involving either physical or emotional abuse with inadequate clinical care or with violation of the principle of autonomy. (⁶)

Trauma: an event or series of events/ circumstances experienced as physically or emotionally harmful or life-threatening with adverse effects on the individual's functioning and wellbeing. (⁷)

Important to distinguish between **postpartum depression** and **PTSD** because they differ in symptoms, treatments and interventions. (⁷)

PTSD is usually treated by stimulating active processing of traumatic material through controlled re-living or eye movement desensitisation reprocessing. However, depression often responds to behavioural activation and cognitive behavioural therapy focused on relations between thought patterns and emotions. (⁷)

PTSD typically entails a **stressful event** which causes the perception of danger to life and triggers development of the disorder - this can be done by **events in the labour room**. (⁸)

2) Database of choice: Ovid Medline.

Key terms include: PTSD, lab*r pain, birth experience*, deliv*, obstetric* analgesi*, postpartum period, health communication.

Results

Type of Result	Key Findings
Biological	Changes associated with the oxytocinergic system are implicated in the response to traumatic events. (10)
(and a second s	Possibility of exogenous oxytocin as a treatment for postpartum PTSD. (10)
(⁹)	Interventions aiming to increase endogenous levels of oxytocin (like improving social and healthcare staff support) may be better at improving PTSD following childbirth (PTSD-FC) with acute trauma in postpartum women. (¹⁰)
Social	A large proportion of midwives are ill-informed on postpartum PTSD. (12)
(11)	Most frequently perceived causes of traumatic birth experiences include: lack and/or loss of control (54.6%), fear for the baby's health/life (49.9%), high intensity pain/discomfort (47.4%) and communication (43.7%). (¹³)
Psychological	Severe postpartum fear of childbirth correlated with symptoms of PTSD and deteriorated quality of life postpartum. (15)
(1 ⁴)	Potential association between emergency c-sections and outcomes like postpartum depression, postpartum PTSD, health-related quality of life (HRQoL), mother-infant bonding, infant feeding, sexual function, self-esteem and fear. (¹⁶)
	Self-blame, rumination and perception of resource loss all significantly associated with post-traumatic stress severity. (17)
Physical	Higher of risk of PTSD in women with unplanned caesarean or vaginal instrumental delivery, reporting more obsessive compulsive, depression and anxiety symptoms. (^{19, 20})
(18)	The events or reasons occurring around a c-section are predictive of PTSD, as well as past maternal complications and avoidance of trauma inflicted by vaginal delivery. (²¹)



Discussion

Interventions aiming to increase levels of endogenous oxytocin (such as improving social [partner] and obstetric staff support) may be superior to exogenous oxytocin treatments in reducing severity of PTSD-FC. (1⁰) Despite this, the all-important question is yet to be answered: can interventions that work to increase endogenous oxytocin levels be used as a preventative measure for PTSD-FC? This is an area future research could delve into.



Interestingly, while poor communication accounted for the lowest percentage for factors perceived to be causal in traumatic birth experiences, it was the most suggested improvement with almost 40% of women wanting things explained and communicated to them better. (13) This insinuates that many factors contributing to a traumatic birth experience are exacerbated by poor communication between the patient and healthcare staff.

Unplanned c-sections and vaginal instrumental deliveries are associated with increased risk of PTSD, perhaps because they are manifestations of a mother's loss of control in how the birth is proceeding - i.e., these procedures were not mapped out in her birth plan. Lack/loss of control was the highest scoring answer for perceived causes of traumatic birth experiences. (13)

Limitations

- Use of studies that used the DSM-IV criteria/DSM-IV adjacent guestionnaires for PTSD diagnosis
- Use of systematic reviews that included studies published more than 5 years ago
- Lack of a bias review for the studies used
- Did not assess for methodological flaws in studies included

Conclusion

Greatest contribution to postpartum PTSD (PP-PTSD) from physical aspects of childbirth due to consequential effects on the:

- appraisal of the birthing experience
- emotions and/or fears of the new mother
- mother's quality of life (including HRQoL) following the birth

Social aspects are a major underlying factor that exacerbate physical obstetric events.

• Preventative measures should focus on improvement in communication between healthcare providers and birth-givers

Reviewing practices in Midwifery and **Obstetrics and Gynaecology** can ensure staff are adequately educated on peri-partum psychological conditions, including their symptoms, presentations and aetiologies.

References

- Rodríguez-Almagro J, Hernández-Martínez A, Rodríguez-Almagro D, Quirós-García JM, Martínez-Galiano JM, Gómez-Salgado J. Women's Perceptions of Living a Traumatic Childbirth Experience and Factors Related to a Birth Experience. International Journal of Environmental Research and Public Health. 2019;16(9): 1654. Available from: doi:10.3390/ijerph16091654
- Tubb A. Only four in 10 people are aware that birth can lead to post-traumatic stress disorder, survey finds. https://maternalmentalhealthalliance.org/news/birth-trauma-ptsd-awareness-survey/ [Accessed 20th June 2022]. Birth Trauma Association. What is birth trauma? https://www.birthtraumaassociation.org.uk/for-parents/what-is-birth-trauma [Accessed 20th June 2022].
- American Psychiatric Association. Postraumatic Stress Disorder. https://www.psychiatry.org/file%20library/psychiatrics/practice/dsm/apa_dsm-5-ptsd.pdf [Accessed 9th June 2022]. Srkalovic Imsiragic A, Begic D, Simicevic L, Bajic Z. Prediction of posttraumatic stress disorder symptomatology after childbirth A Croatian longitudinal study. Women & Birth: Journal of the Australian College of Midwives
- Martinez-Vázquez S, Rodríguez-Almagro J, Hernández-Martínez A, Martínez-Galiano JM. Factors Associated with Postpartum Post-Traumatic Stress Disorder (PTSD) Following Obstetric Violence: A Cross-Sectional Study. Journal of Personalized Medicine. 2021;11(5): 338. Available from: doi:10.3390/jpm11050338
- Personalized Medicine. 2021, 11(2), 330: Available from: 00:1039 (primit road) and a second s 8 Research and Public Health. 2022;19(8): 4900. Available from: doi:10.3390/ijerph19084900
- OpenClipart. From: Free SVG. Female Musculature Line Art. https://freesvg.org/1551737425 [Accessed 27th June 2022].
 Witteveen AB, Stramrood CAI, Henrichs J, Flanagan JC, van Pampus MG, Olff M. The oxytocinergic system in PTSD followi Women's Mental Health. 2020;23(3): 317-329. Available from: doi:10.1007/s00737-019-00994-0 ergic system in PTSD following traumatic childbirth: endogenous and exogenous oxytocin in the peripartum period. [Review]. Archives of
- 11. Mohamed Hassan. From: PxHere. https://pxhere.com/en/photo/1439035 [Accessed 27th June 2022].
- 12. de Vries NE, Stramood CAI, Sligter M, Suijs AM, van Pampus MG. Midwives' practices and knowledge about fear of childbirth and postpartum posttraumatic stress disorder. Women & Birth: Journal of the Australian College of Midwives. 2020;33(1): e95-e104. Available from: doi:10.1016/j.wombi.2018.11.014
- 13. Hollander MH, van Hastenberg E, van Dillen J, van Pampus MG, de Miranda E, Stramrood CAI. Preventing traumatic childbirth experiences: 2192 women's perceptions and views. Archives of Women's Mental Health. 2017;20(4): 515-523. Available from: doi:10.1007/s00737-017-0729-6
- 14. Mohamed Hassan. From: PxHere. https://pxhere.com/en/photo/1440817 [Accessed 27th June 2022].
- Grundström H, Malmquist A, Ivarsson A, Torbjörnsson E, Walz M, Nieminen K. Fear of childbirth postpartum and its correlation sectional study. Archives of Women's Mental Health. 2022;25(2): 485-491. Available from: doi:10.1007/s00737-022-01219-7
- 16. Benton M, Salter A, Tape N, Wilkinson C, Turnbull D, Women's psychosocial outcomes following an emergency caesarean section: A systematic literature review. BMC Pregnancy & Childbirth. 2019;19(1): 535. Available from:
- 17. Tomsis Y, Gelkopf M, Yerushalmi H, Zipori Y. Different coping strategies influence the development of PTSD among first-time mothers. Journal of Maternal-Fetal & Neonatal Medicine. 2018;31(10): 1304-1310. Available from
- 18. Karen Arnold. From: Public Domain Pictures. Pregnant Woman Silhouette Clipart. https://www.publicdomainpictures.n clipart [Accessed 27th June 2022]. ge.php?image=111371&pictur Karen Arnold. From: Public Domain Pictures. Pregnant Woman Silhouette Clipart. https://www.publicdomainpictures.net/en/view-image.php?image=111371&picture=pregnant-woman-silhouette-cli 19. Forray A, Yonkers KA. The Collision of Mental Health, Substance Use Disorder, and Suicide. Obstetrics & Gynecology. 2021;137(6): 1083-1090. Available from: doi:10.1097/AOG.0000000000004391
- 20. Hernandez-Martinez A, Rodriguez-Almagro J, Molina-Alarcon M, Infante-Torres N, Donate Manzanares M, Martinez-Galiano JM. Postpartum post-traumatic stress disorder: Associated perinatal factors and quality of life. Journal of Affective Disorders. 2019;249143-150. Available from: doi:10.1016/j.jad.2019.01.042
- Lopez U, Meyer M, Loures V, Iselin-Chaves I, Epiney M, Kern C, et al. Post-traur Outcomes. 2017;15(1): 118. Available from: doi:10.1186/s12955-017-0692-y ic stress disorder in parturients delivering by caesarean section and the implication of anaesthesia: a prospective cohort study. Health & Quality of Life

A REVIEW OF THE LITERATURE:

AS TO HOW EMOTIONAL DYSREGULATION CAUSED BY POST TRAUMATIC STRESS DISORDER IMPACTS HEART RATE VARIABILITY

June 2022

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Introduction

- Post traumatic stress disorder (PTSD) is a debilitating mental health condition that has a prevalence of around 3% in general population of the UK [⁵]
- It is characterised by re-experiencing a traumatic event.
- It impacts both physical and psychological characteristics.
- PTSD not only affects quality of life but also increases the risk of suicide. [1]

Current treatment issues:

- Trauma-focused therapies are currently the recommended first line treatments for PTSD, but up to **two thirds** maintain a PTSD diagnosis after therapy. [²]
- It is often not diagnosed and treated in a timely matter due to the overlapping symptoms and the tendency of clinicians to inadequately investigate it. [1]

Through a better understanding of PTSD, we can develop more **effective novel therapies** and **improve screening** for PTSD to identify those that need it, which is where heart rate variability comes into play.

PTSD is a serious public health problem that places heavy burdens on individuals and society.

Define key concepts

• Emotional regulation

This is a key concept underlying many mental health conditions including PTSD. Many of the symptoms of PTSD are due to **emotional dysregulation** e.g., hyperarousal to threat, poor regulation of negative emotional states such as sadness or anger. [²]

• The autonomic nervous system

Parasympathetic nervous system

Autonomic nervous system

Sympathetic nervous system 🖌

• Heart rate variability

HRV is a measure of the variation in time between each heartbeat. [7]

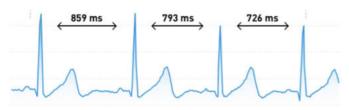


Figure 1 [⁹] Electrocardiogram demonstrating Heart Rate Variability

It is regulated by the parasympathetic nervous system through the vagus nerve. So, it is a useful indicator of **parasympathetic activity**. When HRV is high there is high parasympathetic activity and vice versa.

Low HRV is an indicator of **poor physical health**, in particular cardiovascular disease, as well as **poor mental health**, such as depression and anxiety.

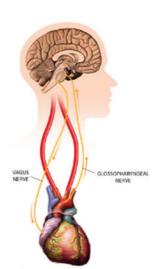


Figure 2 ^{[6}] Diagram showing the vagus nerve

PTSD Chronic and recurrent stress leading to emotional dysregulation Sympathetic hyper activity Supressed parasympathetic activity Low vagel tone Low HRV



SPH

Heart rate variability parameters [⁴]				
Time-domain: quantify the amount of variability in measurements of the time between successive heartbeats	Frequency-domain: measurements estimate the distribution of power or energy in the heart beats			
 Root mean square of successive differences (RMSSD) Standard deviation of NN intervals (SDNN) 	 High frequency (HF-HRV; 0.15-0.40 Hz) Low frequency (LF-HRV; 0.04-0.15 Hz) LF/HF ratio 			

HRV is the most used measure of autonomic nervous system activity because it is non-invasive as well as easy and inexpensive to monitor.

Findings

Almost all of the studies we looked at showed that PTSD was associated with low HRV.

	F	TSD		H	ealth-con	trols		SMD	SMD
Study subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, random, 95% CI	IV, random, 95% CI
Blechert et al.66	5.36	0.88	23	6.16	1.17	32	6.9%	-0.74 (-1.30, -0.19)	
Chang et al. ³⁶	5.07	1.13	32	5.75	1.1	192	7.1%	-0.61 (-0.99, -0.24)	-
Cohen et al.33	4.57	3.97	14	6.01	5.66	25	6.8%	-0.27 (-0.93, 0.38)	
Cohen et al.64	0.12	0.024	9	0.18	0.04	9	6.2%	-1.73 (-2.86, 0.61)	
Ray et al.46	315.89	509.96	41	657	777	41	7.0%	-0.51 (-0.95, -0.07)	
Keary et al.67	3.8	0.4	20	3.6	0.5	20	6.8%	0.43 (-0.19, 1.06)	1
Lakusic et al. ³⁰	4.56	4.62	34	4.82	4.73	34	7.0%	-0.05 (-0.53, 0.42)	
Meyer et al.73	896	796	18	2,509	2,903	23	6.8%	-0.71 (-1.34, -0.07)	
Moon et al.37	157.56	31.99	34	332.83	36.07	27	6.3%	-5.11 (-6.18, -4.05)	
Park et al.71	3.5	0.2	45	4.2	0.2	43	6.8%	-3.47 (-4.14, -2.80)	_
Shah et al.72	4.96	0.83	31	5.33	0.91	385	7.1%	-0.41 (-0.78, -0.04)	
Slewa-Younan et al.69	324.08	98.95	12	875.7	134.9	23	5.9%	-4.34 (-5.63, -3.06) 🖌	
Thome et al.70	6.35	0.19	57	41	6.93	25	5.6%	-9.03 (-10.53, -7.54)	
Tucker et al.35	6,736.2	15,288.4	13	1,210.2	2,636.7	32	6.8%	0.65 (-0.01, 1.31)	+
Wahbeh and Oken ³²	237.9	438.6	52	236.9	395.9	29	7.0%	0.00 (-0.45, 0.46)	
Total (95% CI)		4	35			940	100.0%	-1.58 (-2.32, -0.84)	· •
Heterogeneity: Tau2=1.99,	chi2=334.91, df	=14 (p<0	0.0000)1), I ² =9	6%				-4 -2 0 2 4
Test for overall effect: Z=4.	18 (p<0.0001)								Lower-HRV Greater-HRV

Figure 3. Standard mean difference in HF-HRV between individuals with PTSD and healthy controls taken from a meta-analysis [1]

SMD: standard mean difference, HF-HRV: high-frequency heart rate variability, PTSD: posttraumatic stress disorder.

• Exposure to chronic threat in PTSD may change the function of the vagus nerve causing the low HRV.

Individual with PTSD may constantly perceive threats and experience fear because of **disinhibition of the threat circuits** [¹¹]. They may also have impaired reactions to stressful events characterised by emotional dysregulation.

• Inflammation in the brain found in patients with PTSD may be mediating the association with HRV.

There is increased inflammation in patients with PTSD, which has been shown to potentially change brain structure and function. The inflammation in PTSD was found in amygdala and the dorsomedial prefrontal cortex, which are areas of the brain that have been found to be related to HRV. Therefore, a reduction of HRV may be considered as an indicator for PTSD, due to increased inflammation and changes in brain structure and function. HRV could play a role in the diagnosis and treatment of PTSD and maybe as a biomarker in research. [1]

• Behavioural health factors may account for much of the association between PTSD and HRV. Whilst most studies show an association between low HRV and PTSD, however when some accounted for the following three behavioural health factors there was no longer any correlation; **cigarette consumption**, **history of alcohol dependence**, **and sleep disturbance**. They accounted for **95%** of the shared variation. [⁸]



Figure 4 [10] Diagram showing areas where inflammation can be found in people with PTSD

Conclusion

- These finding only emphasise the negative impact of PTSD on health.
- There is a growing research showing the **negative association** between HRV and PTSD.
- HRV could potentially be used as a useful biomarker to monitor PTSD and its treatment in the future.
- The study exploring the behaviour confounding factors highlights how interventions for individuals with PTSD aimed at smoking and alcohol cessation as well as sleep improvement could have meaningful, long-term benefits, both psychiatric and cardiovascular.

Limitations

- The key limitation is that none of the papers I looked at were able to identify the directionality of the association; if lower HRV is a risk factor for developing PTSD, or if lower HRV is a factor that develops due to PTSD. This is because of the cross sectional nature of the data; to examine the role of HRV further, longitudinal studies are needed. [3]
- Most of the articles did not report the trauma type or looked at people who had experienced different traumas.^[1]
- Since there are many HRV parameters different studies found that different paraments were associated and that others were not. Perhaps a more standardised method of calculating HRV would be better.
- I looked at 5 papers given the time and team member constraints.
- Areas for future study are a longitudinal study on HRV and PTSD as well as how vagal innervation could potentially be a treatment for PTSD.

References

- 1. Ge, F., Yuan, M., Li, Y. and Zhang, W. (2020). Posttraumatic Stress Disorder and Alterations in Resting Heart Rate Variability: A Systematic Review and Meta-Analysis. Psychiatry Investigation, 17(1), pp.9-20. doi:10.30773/pi.2019.0112. Available from :https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6992856/
- Mathersul, D.C., Dixit, K., Schulz-Heik, R.J., Zeitzer, J.M. and Bayley, P.J. (2022). Emotion dysregulation and heart rate variability improve in US veterans undergoing treatment for posttraumatic stress disorder: Secondary exploratory analyses from a randomised controlled trial. BMC Psychiatry, 22(1). doi:10.1186/s12888-022-03886-3. Available from :https://www.researchgate.net/ publication/359983650_Emotion__dysregulation_and_heart_rate_variability_improve_in_US_veterans_undergoing_treatment_for_posttraumatic_stress_disorder_Secondary_exploratory_analyses_from_a_randomised_controlled_trial
- 3. Schneider, M. and Schwerdtfeger, A. (2020). Autonomic dysfunction in posttraumatic stress disorder indexed by heart rate variability: a meta-analysis. Psychological Medicine, pp.1-12. doi:10.1017/s003329172000207x. Available from rnals/psychological-medicine/article/autonomic-dysfunction-in-posttrau dexed-by-heart-rate-variability-a-metaanalysis/777778EA3BEEDC3DF66A9F24F975F4DB https://www.cambridge.org/
- 4. Shaffer, F. and Ginsberg, J.P. (2017). An Overview of Heart Rate Variability Metrics and Norms. Frontiers in Public Health, [online] 5(258). doi:10.3389/fpubh.2017.00258. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC5624990
- 5. Post-Traumatic Stress Disorder (PTSD). (n.d.). [online] Available at: https://www.healthysuffolk.org.uk/uploads/PTSD.pdf
- Image taken from https://www.cainigmedical.com/prolotherapy-news/hrv/
 Campos, M. (2017). Heart rate variability: A new way to track well-being Harvard Health Blog. [online] Harvard Health Blog. Available at: https://www.health.harvard.edu/blog/heart-rate-variability-new-way-track-well-2017112212789.
 Dennis, P.A., Watkins, L., Calhoun, P.S., Oddone, A., Sherwood, A., Dennis, M.F., Rissling, M.B. and Beckham, J.C. (2014). Posttraumatic Stress, Heart-Rate Variability, and the Mediating Role of Behavioral Health Risks. Psychosomatic medicine, [online] 76(8), pp.629-637. doi:10.1097/PSY.00000000000110. Available from https://www.cbi.nlm.nih.gov/pmc/articles/PMC4197067/
- Image taken from https://www.whoop.com/thelocker/heart-rate-variability-hrv/
- 10. Image taken from https://www.researchgate.net/figure/Schematic-overview-of-brain-regions-commonly-affected-in-conduct-disorder-amygdala_fig1_319038032
- Liddell, B.J., Kemp, A.H., Steel, Z., Nickerson, A., Bryant, R.A., Tam, N., Tay, A.K. and Silove, D. (2016). Heart rate variability and the relationship betwee Psychiatry, 16(1). doi:10.1186/s12888-016-0850-5. Available from : https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-016-0850-5 auma exposure age, and psychopathology in a post-conflict setting. BMC





FURTHER READING: NEUROFEEDBACK

The DecNef collection, fMRI data from closed-loop decoded neurofeedback experiments



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Author:	Aurelio Cortese, Saori C. Tanaka, Kaoru Amano, Ai Koizumi,
	Hakwan Lau, Yuka Sasaki, Kazuhisa Shibata, Vincent
Full Article:	Taschereau-Dumouchel, Takeo Watanabe & Mitsuo Kawato www.nature.com/articles/s41597-021-00845-7

Decoded neurofeedback (DecNef) is a form of closed-loop functional magnetic resonance imaging (fMRI) combined with machine learning approaches, which holds some promises for clinical applications. Yet, currently only a few research groups have had the opportunity to run such experiments; furthermore, there is no existing public dataset for scientists to analyse and investigate some of the factors enabling the manipulation of brain dynamics. We release here the data from published DecNef studies, consisting of 5 separate fMRI datasets, each with multiple sessions recorded per participant. For each participant the data consists of a session that was used in the main experiment to train the machine learning decoder, and several (from 3 to 10) closedloop fMRI neural reinforcement sessions. The large dataset, currently comprising more than 60 participants, will be useful to the fMRI community at large and to researchers trying to understand the mechanisms underlying non-invasive modulation of brain dynamics. Finally, the data collection size will increase over time as data from newly run DecNef studies will be added.

Background & Summary

Neurofeedback, based on both functional magnetic resonance imaging (fMRI) and non-fMRI techniques, has seen a dramatic increase in the number of published studies in the last decade1. Decoded neurofeedback (DecNef), a form of closed-loop fMRI neurofeedback combined with machine learning approaches, is a more fine-grained rendering of the long-held goal of manipulating brain dynamics or representations. As opposed to univariate approaches, where one measures the overall activity level within a region-of-interest (ROI), by treating each voxel in isolation, multivoxel pattern analysis (MVPA) is based on algorithms that learn to decode information distributed in patterns of activity. Because DecNef leverages MVPA, rather than using univariate approaches, it has high target specificity. Furthermore, while participants know that a neurofeedback experiment is taking place, they are unaware of the content and purpose of the manipulation - reducing confounds due to cognitive processes, or knowledge about the manipulated dimension. In its most recent declination, the experimenter can even infer the target neural representation indirectly from surrogate participants through a method called hyperalignment.With such a functional alignment approach, patterns of neural activity across participants are used to construct a common, high-dimensional space through a set of linear transformations.

These transformations are effectively parameters, and can be used to bring any new data patterns to/from an individual's brain coordinate system and the model space coordinates.

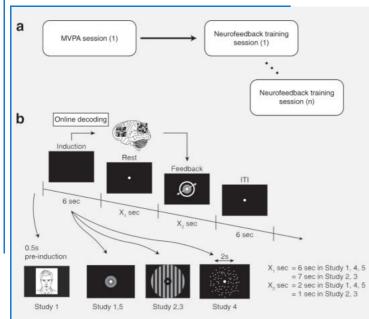
These aspects make DecNef an attractive tool to develop novel clinical applications, particularly in the context of neuropsychiatric disorders. Besides clinically-oriented studies, DecNef can be used as an important paradigm in systems and cognitive neuroscience to study basic functions of the brain.

Several DecNef experiments have been completed to date, targeting representations and cognitive or psychological processes at different levels of the cortical hierarchy: vision and perceptual learning in early visual cortex, subjective preference in cingulate cortex, as well as perceptual confidence in a frontoparietal network.

Briefly, the goal of each study contained in this data collection was to target and non-invasively modulate a specific representation in the brain. Notwithstanding that each experiment probed a different cognitive process or mental representation, all studies used the same basic design logic (Fig. 1a):

(1) an initial session to acquire fMRI data that was used to train the machine learning algorithm - the MVPA or decoder construction session;

2) subsequent neurofeedback sessions, ranging from 2 to 5 days, depending on the study (described in detail in the "Data Records" section). In the decoder construction session, participants performed a simple visual (Study 2, 3), preference (Study 1), perceptual (Study 4), or memory task (Study 5), depending on the study target, while in the neurofeedback sessions the procedure was nearly identical in all cases (Fig. 1b). During neurofeedback training, participants were instructed to modulate or manipulate their brain activity in order to maximize the size of a feedback disc shown on the screen towards the end of each trial. The size of the disc reflected the amount of reward obtained on that single trial (maximum JP¥300), which was then summed to a terminal reward. Participants



N.B.: The visual stimulus presented during the induction period depended on each study

Schematic overview of the experimental design(s). (a) Each study had a first fMRI session dedicated to acquire the data necessary to construct a 'decoder', a machine learning classifier of brain activity patterns.

As of yet, only a few research groups worldwide have had the opportunity to run such technically challenging experiments. We have published elsewhere a description on how to run decoded neurofeedback experiments10. Nevertheless, a key aspect of DecNef (and neurofeedback in general) remains rather elusive: what is the underlying neural mechanism? Recent work has begun to explore this question through experiments, meta-analyses, computational models, and neural network simulations. Reinforcement learning has been suggested as one plausible mechanism, but the field would considerably benefit from having access to a rich dataset, comprising more than 60 individuals and totalling more than 200 hours of fMRI scanning time under DecNef training. This data collection consists of 5 independent studies that shared the same overall



were told that the goal of the task was to maximize the amount of reward (bonus of up to JP¥3000, on top of JP¥8000). Unbeknownst to them, what really determined the size of the feedback disc - and therefore the amount of reward - was the likelihood that their current brain state corresponded to a target state. That is, the previously trained decoder was used in real time to infer how likely it was that a target activity pattern had occurred.

(b) All studies shared the same basic trial design: a first period of 6 seconds called 'induction', during which participants were instructed to "modulate, or change their brain activity in order to maximize the feedback received later in the trial". Unbeknownst to participants, brain activity patterns were fed to the previously trained decoder to calculate the likelihood that the current brain state corresponded to the target state. The likelihood was fed back to participants in the form of a disc within a circle: the larger the disc, the larger the obtained reward. The circle indicated the maximum attainable reward. Beyond this basic structure, the design was slightly modified to meet the requirement of each individual study. In study 1, a neutral face was presented for 0.5 second before the onset of the induction period. Note that in the original study actual face images were used, not cartoons. In study 2 and 3, instead of a simple visual cue indicating the induction period, participants were presented with an achromatic grating. Lastly, in study 4, a random dot kinetogram with 0% coherence was shown for 2 seconds at variable onsets during the induction period.

experimental design. Table 1

(https://www.nature.com/articles/s41597-021-00845-7 /tables/2) summarises all studies, indicating the relevant publication(s), and the main target of the neurofeedback process training.

Finally, it is important to highlight the future growth potential of the DecNef data collection. Besides data generated through our own collaborative efforts, we have recently released software to perform DecNef experiments, under agreement terms that all data shall be made available to the wider scientific community through the DecNef data collection. As such, this cross-country scientific effort will result in new datasets being added semi-automatically to this data sharing project.

Decoded Neurofeedback: Nonconscious Brain Modulation To Remove Fears & Increase Confidence



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Author:	By ATR Brain Information Communication Research Laboratory
Full Article:	Group www.scitechdaily.com/decoded-neurofeedback-nonconscious -brain-modulation-to-remove-fears-increase-confidence/

In recent years, researchers have discovered ways to remove specific fears from the brain, increase one's own confidence, or even change people's preferences, by using a combination of artificial intelligence and brain scanning technology. Their technique could lead to new treatments for patients with conditions such as post-traumatic stress disorder (PTSD), phobias or anxiety disorders.

But while this technique is extremely promising, in some individuals it remains unsuccessful. Why are there such differences in outcome? Better understanding how the brain can self-regulate its own activity patterns would go a long way toward establishing the technique for clinical use. The researchers who spearheaded this technique have thus released a unique dataset (which includes five different studies) to the community, in a bid to accelerate the translation from basic science to application.

The technique is called 'Decoded Neurofeedback', and is based on a method to read and identify specific information in the brain - for example, a fear memory. Dr. Mitsuo Kawato, Director of the Computational Neuroscience Laboratories at the ATR Institute International in Japan, and senior author on the paper and who pioneered the technique a decade ago, explained: "In Decoded Neurofeedback experiments, brain scanning is used to monitor activity in the brain, and identify complex patterns of activity that resemble a specific memory or mental state. When the pattern is detected, we give our experimental participants a small reward. The simple action of repeatedly providing a reward every time the pattern is detected modifies the original memory or mental state. Importantly, participants do not need to be aware of the patterns' content for this to work."

Dr. Aurelio Cortese, senior researcher at ATR Institute International and lead author of the paper, explained the vision for releasing the data: "The Decoded Neurofeedback approach could have major benefits for clinical populations over traditional treatments. Patients could avoid the stress associated with exposure therapies, or side-effects resulting from established drugs. As such, it is crucial we accelerate the development of the Decoded Neurofeedback technique – and this will only be possible if more scientists will be able to work on the actual data."



The research group has constructed a valuable neuroimaging database of more than 60 individuals who underwent Decoded Neurofeedback training. This database consists of structural images of the brain, functional images of the brain, machine learning decoders, and additional processed data. Anyone who wants to use the dataset must apply through the ATR institutional repository or Synapse, an online repository of neuroscientific data. The details on how to access the dataset are specified in the original publication as well as on the ATR and Synapse websites.

Reference: "The DecNef collection, fMRI data from closed-loop decoded neurofeedback experiments" by Aurelio Cortese, Saori C. Tanaka, Kaoru Amano, Ai Koizumi, Hakwan Lau, Yuka Sasaki, Kazuhisa Shibata, Vincent Taschereau-Dumouchel, Takeo Watanabe and Mitsuo Kawato, 23 February 2021, Scientific Data. DOI: 10.1038/s41597-021-00845-7SciTechDaily

Biofeedback shows promise as mental health treatment



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Author:	Lori Uildriks, Pharm.D., BCPS, BCGP
Full Article:	www.medicalnewstoday.com/articles/biofeedback-shows-pro
	mise-as-mental-health-treatment#Novel-treatment-method

- A recent meta-analysis has demonstrated some positive results using real-time functional MRI neurofeedback (rtfMRI-NF) in treating various mental illnesses.
- The reviewed studies showed that participants could use a neurofeedback signal and self-regulate brain activity in targeted areas.
- While the data demonstrated that rtfMRI-NF had a moderate effect on neural activity in targeted brain regions during training, the researchers observed a more significant effect later, in the absence of a neurofeedback signal.
- However, the review found that rtfMRI-NF had only a small effect on behavioral outcomes. More research on how rtfMRI-NF works, and for whom it is most effective, is necessary to establish its clinical usefulness outside of a research setting.

Mental health conditions can cause changes in thinking, emotions, behavior, or all of these, impairing interpersonal relationships and daily functioning. They can be temporary or chronic.

Approximately 26% of adults in the United States will experience a mental health condition within a given year, with close to 9.5% having a serious condition, such as major depression or bipolar disorder.

Although pharmacologic and psychosocial treatment options for psychiatric illnesses can be safe and effective, there are cases in which the treatments may cause significant adverse effects in some individuals, potentially leading to discontinuation. In addition, some illnesses are treatment-resistant.

One possible reason why current standard-of-care treatments have varying efficacy is that they do not target the disruption to neural circuits that researchers have associated with mental illness.

Researchers can use functional MRI (fMRI), a noninvasive neuroimaging tool that measures brain activity through changes in cerebral blood flow, to comprehend the neurobiological changes accompanying psychiatric illness.

In the new study, the researchers used rtfMRI-NF, which

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incorporates biofeedback, to teach the participants how to control their own brain neural activity instantaneously while in a scanner. Biofeedback is a treatment that healthcare professionals sometimes use to control involuntary bodily processes.

Novel treatment method

Although some studies using rtfMRI-NF experimentally to treat a wide range of mental illnesses have demonstrated benefits, rtfMRI-NF is costly, and it requires extensive setup for real-time analysis.

Researchers at the University of Rochester Medical Center in New York conducted a meta-analysis of 17 relevant studies to determine the effectiveness of rtfMRI-NF in modulating brain activity and behavioral outcomes.

They have published their findings in Neuroscience & Biobehavioral Reviews.

Study co-author Dr. David Dodell-Feder, an assistant professor at both the Department of Psychology in the School of Arts and Sciences at the University of Rochester and the Department of Neuroscience at the University's Medical Center, comments on the objectives of the review: "Ultimately, we want people to be able to take what they learn in the scanner during the training sessions to use in their day-to-day life. If they can do that, it shows that the neurofeedback is meaningful, that they are taking something away from it, and that they can now apply that experience – even without neurofeedback."

The meta-analysis evaluated whether rtfMRI-NF led to voluntary control of brain activity during training, whether the effects persisted after training (in the absence of neurofeedback), and whether treatment resulted in improved outcomes.

The studies that the team analyzed included 410 participants, of whom 234 received rtfMRI-NF. The study participants were 34 years old, on average, and there were almost equal numbers of males and females. About 53% of the participants took psychotropic medications.

The studies included participants with diagnoses such as:

- depressive disorders
- schizophrenia and other psychotic disorders
- neurodevelopmental disorders
- substance-related and addictive disorders
- trauma and stressor-related disorders
- anxiety disorders



The study participants completed an average of two sessions with a total regulation time of about 24 minutes across sessions. Most studies compared active neurofeedback with a sham feedback control group.

The area of the brain targeted most often as the source of the neurofeedback signal was the amygdala. The amygdala is part of the brain's limbic system, and it is responsible for processing strong emotions, such as fear and pleasure.

Additionally, most studies provided explicit instructions for regulating the neural signal, measured the percent signal-change that a task triggered, provided continuous neurofeedback, and included a transfer task to measure whether the participant could perform the previously learned regulation during the period of no neurofeedback.

Some positive results

The meta-analysis found that rtfMRI-NF produced a moderate effect on the brain activity of targeted regions during training and a large effect after training in the absence of neurofeedback.

However, rtfMRI-NF demonstrated only a small effect on symptoms and cognitive impairment.

Emily Dudek, lead author and a clinical research coordinator at the Brain Injury Research Center of Mount Sinai in New York City, comments on the results:

"We believe this provides relatively strong evidence that volitional control over neural processes that are specifically targeted during training is possible. This volitional control was also present in contexts in which no feedback was provided," she notes.

The possibility of publication bias – the influence of nonpublished studies that failed to find an effect – that the team detected during analyses may further decrease the measured effect of rtfMRI-NF on symptoms.

Limitations of the meta-analysis include small study sample sizes leading to potential underpowering and decreased validity of results.

Further research involving adequately powered, high quality studies is necessary to elucidate specifically how and for whom rtfMRI-NF demonstrates effectiveness to optimize potential clinical benefits. Future studies may be crucial to proving the clinical utility of rtfMRI-NF outside a research setting.

Prof. Dodell-Feder, Dr. J. Steven Lamberti, from the Department of Psychiatry at the University of Rochester Medical Center, and a graduate student team have set out to conduct a rtfMRI-NF research study aiming to teach people with schizophrenia to self-regulate areas of the brain responsible for social information processing.

The trial is ongoing, and, hopefully, the results of the study will provide some much-needed answers.



Neurofeedback Therapy of Attention Deficits in Patients with Traumatic Brain Injury

Background. Impairments of attention are a frequent and well documented consequence of head injury. The purpose of this study was to evaluate if Neurofeedback Therapy (NFT) can enhance remediation of attention deficits in patients with closed head injuries (CHI) who are still in the phase of spontaneous recovery. Method. Feedback of beta-activity (13-20 Hz) was used for the treatment of attentional impairments in twelve patients with moderate closed head injuries. A matched control group of nine patients was treated with a standard computerized training. All patients were tested before and after treatment with a set of attention tests. Results. After ten sessions the analyses of beta activity showed that eight patients were able to increase their beta activity while the remaining four patients showed a decrease of beta activity. Mean duration of beta activity was prolonged about 50% after training. Patients who received NFT improved significantly more in the attention tests than control patients. Conclusion. The results suggest that neurofeedback is a promising method for the treatment of attentional disorders in patients with traumatic brain injuries. It is suggested that NFT should focus not only on the enhancement of beta activity, but also on the duration patients are able to hold beta activity. It is proposed to use NFT also with patients in the early phase of rehabilitation.

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Author:	Ingo Keller
Full Article:	doi.org/10.1300/J184v05n01_03

Attention and Neurofeedback Synchrony Training: Clinical Results and Their Significance

Background. Impairments of attention are a frequent and well documented consequence of head injury. The purpose of this study was to evaluate if Neurofeedback Therapy (NFT) can enhance remediation of attention deficits in patients with closed head injuries (CHI) who are still in the phase of spontaneous recovery. Method. Feedback of beta-activity (13-20 Hz) was used for the treatment of attentional impairments in twelve patients with moderate closed head injuries. A matched control group of nine patients was treated with a standard computerized training. All patients were tested before and after treatment with a set of attention tests. Results. After ten sessions the analyses of beta activity showed that eight patients were able to increase their beta activity while the remaining four patients showed a decrease of beta activity. Mean duration of beta activity was prolonged about 50% after training. Patients who received NFT improved significantly more in the attention tests than control patients. Conclusion. The results suggest that neurofeedback is a promising method for the treatment of attentional disorders in patients with traumatic brain injuries. It is suggested that NFT should focus not only on the enhancement of beta activity, but also on the duration patients are able to hold beta activity. It is proposed to use NFT also with patients in the early phase of rehabilitation.

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Author:	McKnight, J.T., & Fehmi, L.G
Full Article:	doi.org/10.1300/J184v05n01_05



Biofeedback treatments of generalized anxiety disorder: Preliminary results

Background. Impairments of attention are a frequent and well documented consequence of head injury. The purpose of this study was to evaluate if Neurofeedback Therapy (NFT) can enhance remediation of attention deficits in patients with closed head injuries (CHI) who are still in the phase of spontaneous recovery. Method. Feedback of beta-activity (13-20 Hz) was used for the treatment of attentional impairments in twelve patients with moderate closed head injuries. A matched control group of nine patients was treated with a standard computerized training. All patients were tested before and after treatment with a set of attention tests. Results. After ten sessions the analyses of beta activity showed that eight patients were able to increase their beta activity while the remaining four patients showed a decrease of beta activity. Mean duration of beta activity was prolonged about 50% after training. Patients who received NFT improved significantly more in the attention tests than control patients. Conclusion. The results suggest that neurofeedback is a promising method for the treatment of attentional disorders in patients with traumatic brain injuries. It is suggested that NFT should focus not only on the enhancement of beta activity, but also on the duration patients are able to hold beta activity. It is proposed to use NFT also with patients in the early phase of rehabilitation.

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Author:	Kathleen M. Rice, Edward B. Blanchard
Full Article:	doi.org/10.1007/BF01848110

The Efficacy of Neurofeedback in Patients with Major Depressive Disorder: An Open Labeled Prospective Study

The purpose of this study was to evaluate the effect of neurofeedback on depressive symptoms and electrophysiological disturbances in patients with major depressive disorder. We recruited participants suffering from depression to evaluate efficacy of left prefrontal beta with alpha/theta training. An 8-week, prospective, open-label study was undertaken. Twenty participants were recruited. The treatment protocol was twice or three times a week training of beta at F3 with alpha/theta at Pz for 8 weeks. When every visit, patients were received beta training for 30 min, and then alpha/theta training for 30 min. Baseline, 4 and 8 week scores of; the Hamilton rating scale for Depression (HAM-D), the Hamilton rating scale for Anxiety (HAM-A), the Beck Depression Inventory (BDI)-II, the Beck Anxiety Inventory (BAI), Clinical global impression-severity (CGI-S), and pre- and post-treatment resting state EEGs were compared. Interhemispheric alpha power asymmetry (A score) was computed for homologous sites F3-F4. Pre- and post-training clinical assessments revealed significant improvements in HAM-D, HAM-A, BDI, and CGI-S scores. Cumulative response rates by HAM-D were 35.0 and 75.0 % at 4 and 8 weeks, respectively, corresponding cumulative remission rates by HAM-D were 15.0 and 55.0 %, respectively. No significant differences were found between pre- and post-treatment A score. Neurofeedback treatment could improve depressive symptoms significantly. In addition, anxiety symptoms and clinical illness severity decreased significantly after neurofeedback treatment. Despite its several limitations, such as, small sample size and lack of a control group, this study suggested neurofeedback has significant effects in patients with major depressive disorder.

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Author:	Eun-Jin Cheon, Bon-Hoon Koo & Joong-Hyun Choi
Full Article:	doi.org/10.1007/s10484-015-9315-8

Neurofeedback Treatment of Depression and Anxiety



A robust body of research documents that there are biological predispositions that often exist for depression, anxiety, and obsessive-compulsive disorder. However, new research has shown that medication is only mildly more effective than placebo in the treatment of these problems. In treating these conditions, neurofeedback (EEG biofeedback) may offer an alternative to invasive treatments such as medication, ECT, and intense levels of transcrancial magnetic stimulation. This paper reviews the neurofeedback literature with these problems, finding particularly positive research support for the treatment of anxiety disorders. New findings on the neurofeedback treatment of depression are presented.

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	pages131-137(2005)
Author:	D. Corydon Hammond
Full Article:	doi.org/10.1007/s10804-005-7029-5

A Systematic Review of the Effect of Neurofeedback in Cancer Patients

Altogether, there is initial evidence that NF is a complementary, drug-free, and noninvasive therapy that has the potential to ameliorate symptoms in this patient group, such as pain, fatigue, depression, and sleep. Further studies are highly needed.

	Published in:	Integrative Cancer Therapies, Volume 18(1): 1-13 (2019)
	Author:	Madeleine Hetkamp, Jasmin Bender, Nadine Rheindorf, Axel
		Kowalski, Marion Lindner, Sarah Knispel, Mingo Beckmann,
ļ		Sefik Tagay, and Martin Teufel
	Full Article:	doi.org/10.1177/1534735419832361

An Overview Of Alpha-Theta Neurofeedback And Its Treatment Effectiveness For Substance Abuse

Neurofeedback, has been used successfully for the treatment of substance abuse for over 25 years. Built on the work of Kamiya and Green (Budzynski, 1999), Eugene Peniston published a series of papers using alpha-theta neurofeedback with a Veteran's Administration (VA) population of Vietnam War veterans diagnosed with alcohol abuse and post-traumatic stress disorder (PTSD) (Peniston & Kulkosky, 1989; Peniston & Kulkosky, 1990; Peniston, Marrinan, Deming, & Kulkosky, 1993). These important 'Peniston papers' no doubt facilitated a wave of EEG practitioners who rely on alpha-theta neurofeedback, or its modified forms, to treat substance abuse (as well as PTSD) that continues to this day.

Published in:BMED ReportAuthor:Christopher Fisher, PhDFull Article:www.bmedreport.com/archives/6071



Alpha-theta brainwave neurofeedback training: An effective treatment for male and female alcoholics with depressive symptoms

This was an experimental study of 14 alcoholic outpatients using the Peniston and Kulkosky (1989, 1991) brainwave treatment protocol for alcohol abuse. After temperature biofeedback pretraining, experimental subjects completed 20 40-minute sessions of alpha-theta brainwave neurofeedback training (BWNT). Experimentally treated alcoholics with depressive syndrome showed sharp reductions in self-assessed depression (Beck's Depression Inventory). On the Millon Clinical Multiaxial Inventory-I, the experimental subjects showed significant decreases on the BR scores: schizoid, avoidant, dependent, histrionic, passive-aggression, schizotypal, borderline, anxiety, somatoform, hypomanic, dysthmic, alcohol abuse, drug abuse, psychotic thinking, and psychotic depression. Twenty-one-month follow-up data indicated sustained prevention of relapse in alcoholics who completed BWNT.

Published in:	Journal of Clinical Psychology 1995 - 1995;51(5):685-693
Author:	Ellen Saxby Eugene G. Peniston
Full Article:	doi.org/10.1002/1097-4679(199509)51:5%3C685::AID-JCLP2
	270510514%3E3.0.CO;2-K

Online psychotherapy: trailblazing digital healthcare

"There is strong evidence supporting online cognitive-behavioural therapy and more engaging programmes are now appearing so as to reduce user "attrition". The next generation of autonomous psychotherapy programmes will implement adaptive and personalised responses, moving beyond impersonalised advice on cognitive and behavioural techniques. This will be a more authentic form of psychotherapy that integrates therapy with the actual relations experiences of the individual user.

Published in:	Published online by Cambridge University Press: 07
	October 2019
Author:	Annabel McDonald, Jessica A. Eccles, Sanaz Fallahkhair, Hugo
	D. Critchley
Full Article:	doi.org/10.1192/bjb.2019.66
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Alcoholic personality and alpha-theta brainwave training

The Millon Clinical Multiaxial Inventory (MCMI) and the Sixteen Personality Factor Questionnaire (16PF) were employed to assess personality differences and changes among 20 chronic alcoholics and 10 nonalcoholic controls prior to and after either traditional medical treatment (MT) or alpha-theta brainwave (ATB) training of the alcoholics. EEG ATB treatment was accompanied by significant decreases in MCMI scales labeled schizoid, avoidant, passive-aggression, schizotypal, borderline, paranoid, anxiety, somatoform, dysthymia, alcohol abuse, psychotic thinking, psychotic depression, and psychotic delusion. Alcoholics receiving TMT showed significant decreases only in 2 MCMI scales, avoidant and psychotic thinking, and an increase in 1 scale, compulsive. On the 16PF, EEG ATB treatment corresponded to significant increase in warmth, abstract-thinking, stability, conscientiousness, boldness, imaginativeness, and self-control. Alcoholics receiving TMT showed only a significant increase in concrete-thinking. (PsycINFO Database Record (c) 2019 APA, all rights reserved)

Published in:	Medical Psychotherapy: An International Journal, 3, 37-55.
Author:	Peniston, Eugene G., Kulkosky, Paul J.
Full Article:	psycnet.apa.org/record/1994-07253-001



QEEG-Guided Neurofeedback for Recurrent Migraine Headaches

Seventy-one patients with recurrent migraine headaches, aged 17-62, from one neurological practice, completed a quantitative electroencephalogram (QEEG) procedure. All QEEG results indicated an excess of high-frequency beta activity (21-30 Hz) in 1-4 cortical areas. Forty-six of the 71 patients selected neurofeedback training while the remaining 25 chose to continue on drug therapy. Neurofeedback protocols consisted of reducing 21-30 Hz activity and increasing 10 Hz activity (5 sessions for each affected site). All the patients were classified as migraine without aura. For the neurofeedback group the majority (54%) experienced complete cessation of their migraines, and many others (39%) experienced a reduction in migraine frequency of greater than 50%. Four percent experienced a decrease in headache frequency of <50%. Only one patient did not experience a reduction in headache frequency. The control group of subjects who chose to continue drug therapy as opposed to neurofeedback experienced no change in headache frequency (68%), a reduction of less than 50% (20%), or a reduction greater than 50% (8%). QEEG-guided neurofeedback appears to be dramatically effective in abolishing or significantly reducing headache frequency in patients with recurrent migraine.

Published in:	Clinical EEG and Neuroscience, 42(1), 59-61
Author:	Jonathan E. Walker
Full Article:	doi.org/10.1177%2F155005941104200112

Neuromodulation and neurofeedback treatments in eating disorders and obesity

During the last 20 months, seven case studies/series and seven randomized controlled trials (RCTs) of NIBS or neurofeedback in different eating disorders, obesity, or food craving have appeared. These have largely had promising results.

Published in:	Current Opinion in Psychiatry: November 2017 - Volume 30 - Issue 6 - p 458-473
Author:	Dalton, Bethan; Campbell, Iain C.; Schmidt, Ulrike
Full Article:	doi.org/10.1097/yco.000000000000361

Insights in EEG versus HEG and RT-FMRI neuro feedback training for cognition enhancement

Innovative research technologies in the neurosciences have remarkably improved the perception of brain structure and function. The use of several neurofeedback training techniques is broadly used for the memory and cognition augmentation as well as for several learning difficulties and AHDD rehabilitation. Author's objective is to review cognitive enhancement techniques with the use of brain imaging intervention methods as well to evaluate the effects of these methods in the educational process. The efficiency and limitations of neurofeedback training with the use of EEG brain imaging, HEG scanning, namely NIR and PIR method and fMRI scan including rt-fMRI brain scanning technique are also discussed. Moreover, technical and clinical details of several neurofeedback treatment approaches were also taken into consideration

Published in:	International Journal of Artificial Intelligence and
	Applications (IJAIA), Vol. 7, No. 6, November 2016
Author:	Antonia Plerou and Panagiotis Vlamos
Full Article:	doi.org/10.5121/ijaia.2016.7602



Treatment of chronic fatigue with neurofeedback and self-hypnosis

A 21 year old patient reported a relatively rapid onset of serious chronic fatigue syndrome (CFS), with her worst symptoms being cognitive impairments. Congruent with research on rapid onset CFS, she had no psychiatric history and specialized testing did not suggest that somatization was likely. Neuroimaging and EEG research has documented brain dysfunction in cases of CFS. Therefore, a quantitative EEG was done, comparing her to a normative data base. This revealed excessive left frontal theta brainwave activity in an area previously implicated in SPECT research. Therefore, a novel treatment approach was utilized consisting of a combination of EEG neurofeedback and self-hypnosis training, both of which seemed very beneficial. She experienced considerable improvement in fatigue, vigor, and confusion as measured pre-post with the Profile of Mood States and through collaborative interviews with both parents. Most of the changes were maintained at 5, 7, and 9 month follow-up testing.

Published in:	NeuroRehabilitation. 2001;16(4):295-300
Author:	D C Hammond
Full Article:	pubmed.ncbi.nlm.nih.gov/11790917/

Efficacy of neurofeedback treatment in ADHD: the effects on inattention, impulsivity and hyperactivity: a meta-analysis

Since the first reports of neurofeedback treatment in Attention Deficit Hyperactivity Disorder (ADHD) in 1976, many studies have investigated the effects of neurofeedback on different symptoms of ADHD such as inattention, impulsivity and hyperactivity.

Due to the inclusion of some very recent and sound methodological studies in this meta-analysis, potential confounding factors such as small studies, lack of randomization in previous studies and a lack of adequate control groups have been addressed, and the clinical effects of neurofeedback in the treatment of ADHD can be regarded as clinically meaningful. Three randomized studies have employed a semi-active control group which can be regarded as a credible sham control providing an equal level of cognitive training and client-therapist interaction. Therefore, in line with the AAPB and ISNR guidelines for rating clinical efficacy, we conclude that neurofeedback treatment for ADHD can be considered "Efficacious and Specific" (Level 5) with a large ES for inattention and impulsivity and a medium ES for hyperactivity.

Published in:	Clinical EEG and Neuroscience 2009 Jul;40(3):180-9
Author:	Martijn Arns, Sabine de Ridder, Ute Strehl, Marinus Breteler,
	Anton Coenen
Full Article:	doi.org/10.1177/155005940904000311

An Open Clinical Trial Utilizing Real-Time EEG Operant Conditioning as an Adjunctive Therapy in the Treatment of Crack Cocaine Dependence

This study investigated the treatment outcome of males dependent on crack cocaine participating in an inpatient treatment facility in which electroencephalographic operant conditioning training (EEG-OC) was added to the treatment protocol. Eighty-seven men were assessed twelve months after completion of the EEG portion of the program. Follow-up procedures of urinalyses, self-report measures, length of residence, and scores on a measure of depression were obtained and showed significant changes after treatment. The addition of EEG-OC to crack cocaine treatment regimens may promise to be an effective intervention for treating crack cocaine abuse and increasing treatment retention.

Published in:	Journal of Neurotherapy - Vol 9 No 2 (2005) , 27-47
Author:	Virginia Shannon Burkett, John Michael Cummins, Robert
Full Article:	Malcolm Dickson, Malcolm Skolnick doi.org/10.1300/J184v09n02_03
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Alpha Conditioning as an Adjunct Treatment for Drug Dependence: Part I

The effects of alpha conditioning on the habits of four methadone maintained patients were assessed. All four learned some control over alpha activity in the 5-week, 10-session training period. The most striking results, however, related to the subjects' substitution of self-initiated mental states associated with alpha for previously used drug-seeking or self-medicating methods of coping with everday problem situations. All four subject reported a decrease in illicit drug usage and an increased feeling of self-control. Verification of improvement in adjustment and drug abuse was shown by counseling reports and narcotic screens from the maintenance program.

Published in:	International Journal of the Addictions, 11:6, 1085-1089
Author:	Richard J. Goldberg, John C. Greenwood & Zebulon Taintor
Full Article:	doi.org/10.3109/10826087609058830

Neurofeedback Effects on Evoked and Induced EEG Gamma Band Reactivity to Drug-Related Cues in Cocaine Addiction

Our study emphasizes the utility of cognitive neuroscience methods based on EEG gamma band measures for the assessment of the functional outcomes of neurofeedback-based biobehavioral interventions for cocaine use disorders. This approach may have significant potential for identifying both physiological and clinical markers of treatment progress. The results confirmed our prediction that EEG changes achieved with neurofeedback training will be accompanied by positive EEG outcomes in a cue reactivity and clinical improvements.

Published in:	Journal of Neurotherapy - Vol 14 No 3 (2010)
Author:	Timothy Horrell, Ayman El-Baz, Joshua Baruth, Allan Tasman,
	Guela Sokhadze, Christopher Stewart, Estate Sokhadze
Full Article:	doi.org/10.1080/10874208.2010.501498

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