Attachment 3

Summary of Professional Accomplishment

Enhancing Personalization and Effectiveness of Neurofeedback Therapy through Artificial Neural Networks

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Warsaw, May 2023

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1. Name

Jacek Rogala

2. Diplomas, degrees conferred in specific areas of science, including the name of the institution which conferred the degree, year of degree conferment, title of the PhD dissertation

- Master of science, Thesis: Feeding of smelt (osmerus eperlanus) in seven mazovian lakes, Laboratory of Hydrobiology, Faculty of Biology, University of Warsaw 1991
- PhD, Thesis: The role of Perigeniculate Nucleus (PGN) in modulation of response of principal cells in Lateral Geniculate Nucleus (LGN), Laboratory of Neuroinformatics, Institute of Experimenal Biology, Polish Academy of Sciences, 2014

3. Information on employment in research institutes or faculties/ departments or school of arts

- Specialist: Biomedical Physics Division, Faculty of Physics, University of Warsaw (2022-today)
- Neurobiologists: Bioimaging Research Center, World Hearing Center, Institute of Physiology and Pathology of Hearing (2018–2022)
- Postdoctoral fellow: Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń (2017–2018)
- Postdoctoral fellow: Laboratory of Neurobiology of Vision, Department of Neurophysiology, Institute of Experimental Biology (2014–2016)

4. Scientific achievement

4.1. Title of the scientific achievement

Title of the scientific achievement constituting the basis for the habilitation procedure:

Enhancing Personalization and Effectiveness of Neurofeedback Therapy through Artificial Neural Networks

The achievement concerns the study of the mechanism of neurofeedback-EEG as a method of therapy of cognitive disorders based on a personalized protocol using explainable artificial neural networks.

4.2. List of works constituting the basis of the habilitation procedure

The table below presents a list of five publications that form a cohesive series, serving as the foundation for the habilitation procedure. My specific contributions to these publications can be found in the list of publications below as well as in Appendix 3 (List of Achievements).

Authors (year)	Title	Journal
[1] Jacek Rogala, Katarzyna Jurewicz, Katarzyna Paluch, Ewa Kublik, Ryszard Cetnarski, Andrzej Wróbel (2016)	The do's and don'ts of neurofeedback training: a review of the controlled studies using healthy adults	Frontiers in Human Neuroscience, doi.org/10.3389/fnhum.2016.00301. (IF=3.473) MNiSW 100 Citations (WoS): 57
My Contribution: concept, data analyses, main conclusions, article drafting		

[2] Katarzyna Paluch, Katarzyna Jurewicz, **Jacek Rogala**, Rafał Krauz, Marta Szczypińska, Mirosław Mikicin, Andrzej Wróbel, Ewa Kublik (2017)	Beware: Recruitment of Muscle Activity by the EEG-Neurofeedback Trainings of High Frequencies	Frontiers in Human Neuroscience. Volume 11 – 2017. doi.org/10.3389/fnhum.2017.00119 (IF=3.473) MNiSW 100 Citations (WoS): 15
My Contribution: Interpretation of the results, proofreading		
[3] Jacek Rogala, Ewa Kublik, Rafał Krauz, Andrzej Wróbel (2020)	Resting-state EEG activity predicts frontoparietal network reconfiguration and improved attentional performance	Scientific Reports, 10 (2020), pp. 1-15, 10.1038/s41598-020-61866-7 (IF=4.996) MNiSW 140 Citations (WoS): 26
My Contribution: concept, data analyses, main conclusions, article drafting		
[4] Jacek Rogala, Joanna Dreszer, Urszula Malinowska, Marek Waligóra, Agnieszka Pluta, Ingrida Antonova, Andrzej Wróbel (2021)	Stronger connectivity and higher extraversion protect against stress-related deterioration of cognitive functions	Scientific Reports, 11, 17452. (IF=4.996) MNiSW 140 Citations (WoS): 2
My Contribution: concept, data analyses, main conclusions, article drafting		
Jarosław Żygierewicz, Romuald A Janik, Igor T Podolak, Alan Drozd, Urszula Malinowska, Martyna Poziomska, Jakub **[5]** Wojciechowski, Paweł Ogniewski, Paweł Niedbalski, Iwona Terczynska, **Jacek Rogala** (2022)	Decoding working memory-related information from repeated psychophysiological EEG experiments using convolutional and contrastive neural networks	Journal of Neural Engineering 19 046053 DOI 10.1088/1741-2552/ac8b38 (IF=5.043) MNiSW 140 Citations (WoS): 0
My Contribution: concept, data analyses, main conclusions, article drafting		

The content of the publication is included in Appendix No. 5, and the statements of the authors of joint publications (except for [1], [2], [3] and [4], in which there is an Author contribution paragraph) are included in Appendix No. 6.

4.3. Discussion of the scientific achievement

The purpose of the studies described in a series of publications [1-5] was to verify and improve the efficacy of Neurofeedback-EEG (N-EEG) as a technique to support the development/ therapy of cognitive functions. N-EEG is a biological feedback that provides the patient with information (feedback) about his or her brain activity. This information is based on EEG collected in real time using electrodes placed on the patient's head. Then, after processing by a specially designed software, this signal is presented to the patient in the form of graphs, games or sound. During therapy sessions (usually a minimum of 20), the patient is encouraged to influence the activity of his or her brain by using various strategies and techniques, such as meditation, visualization or breath control. If the person achieves the desired changes in his or her brain activity, he or she receives positive feedback, in form of, for example, an increase in pitch or a change in the image on the screen. N-EEG training should lead to the attenuation of undesired and the amplification of desired EEG waves. N-EEG takes advantage of the "plasticity of the brain," relying on the ability of the brain's neuronal networks to consolidate changes in activated connections.

Unfortunately, commonly used N-EEG training methods do not provide satisfactory level of effectiveness [1]. In most cases, the therapy does not contribute to significant improvements in health and well-being of participants, exposing them to unnecessary costs, or even to worsening of their condition, if other therapeutic methods are abandoned at the same time. On the other hand, clinical studies indicate that when improving the cognitive functions of elderly people and those affected by central nervous system disorders, additional behavioral therapy enhances the results of drug treatment.

The low effectiveness of N-EEG therapy is mainly attributed to poorly selected training methods [1]. Current training protocols (electrode placement and selection of the EEG frequency range used for training) are based on analysis of resting-state EEG recordings or comparison of the patient's EEG recordings with those from a normative base. The chosen training protocol is designed to amplify or attenuate the EEG in selected frequency ranges (bands), according to commonly used tables (e.g., Kropotov, 2009). Since the relationship between the amplitude of the selected EEG band and the cognitive function assigned to it (and its dysfunction) has no clear scientific basis, the selection of therapy is often arbitrary and, as a result, the effectiveness of applied N-EEG therapies is low.

The research described in the presented series of publications has allowed the formulation of a novel (one of the first in the world) critical evaluation of existing therapeutic and research practices, and provided the basis for further work towards the development of a new method that allows the preparation of a personalized training protocol using artificial neural networks. These new methods allow for the preparation of a protocol based on personalized analysis of the EEG recorded during the performance of tasks based on targeted cognitive functions. Comparative analysis of EEG recordings collected during the performance of a task related to a given function allows the determination of training parameters, i.e. EEG features accompanying only trials performed correctly. Reinforcement of these features during training also based on tasks using a given function should lead to improved performance as measured by the patient's cognitive abilities.

The primary research challenge was to analytically link the behavioral results collected during a cognitive task to the dynamics of individual EEG maps. Previous attempts have encountered difficulties due to interference from concurrently recorded muscle activity [2], external interference and high variability of the EEG signal. An additional analytical concern was the multidimensionality of the EEG signal (electrode placement, amplitude, frequency, timing, correlations between signals from individual electrodes) and the lack of clear relationships between the EEG and behavior or cognitive function. To identify states of EEG activity during accurately executed trials, we pioneered the utilization of explainable artificial intelligence (XAI) - an innovative branch of artificial intelligence focused on transparency and interpretability. By employing the XAI methodology, we effectively discerned the key features within the EEG that drive the classification process. Subsequently, we proceeded to conduct a comprehensive physiological interpretation of the obtained results. This approach allowed us to gain valuable insights into the underlying mechanisms behind the EEG and its relevance to the classification task. **In the course of our research, we discovered that the relevance of EEG features in the**

classification process depends on the applied neural network training method. This is crucial not only for N-EEG training, which should be based on features with a physiologically known mechanism, but also in medical diagnostics, such as the detection and classification of motor and cognitive disorders. The methods and solutions we have developed may serve as a solid foundation for achieving personalization, objectivity, and automation in training and therapy using the N-EEG. These advancements significantly enhance its effectiveness and yield substantial contributions towards the integration of artificial neural networks in clinical practice.

4.3.1. History of Neurofeedback-EEG (N-EEG) research.

One of the pioneers of N-EEG was Joe Kamiya, who in 1962 discovered that, using a simple device that makes a sound when an increase in alpha band (8-12 Hz) activity is detected, participants can be taught to consciously control the amplitude pitch of this band. Around the same time, Barry Sterman and his team, an important member of which was Wanda Wyrwicka, an alumna of the M. Nencki Institute of Experimental Biology, discovered that cats could be taught to increase the amplitude of the sensorimotor rhythm (SMR; 12-15Hz) recorded over the motor cortex (Sterman et al. 1969). Directly rewarding an increase in SMR rhythm activity, accompanied by a decrease in motor activity, proved to be a more effective than rewarding the body's immobility response. It also appeared that cats trained to increase SMR activity were more resistant to seizures induced by pharmacological agents. This discovery contributed to the development of the first neurofeedback protocol (i.e., determining the trained frequency and electrode placement) for seizure disorders in humans (Sterman and Friar 1972). A little later, Joel Lubar, published the first article describing the use of neurofeedback in the treatment of hyperactivity (Lubar and Shouse 1976). Since then, the number of publications devoted to N-EEG has steadily increased. In the first two decades (1972-1990), 162 papers on N-EEG were published (data based on a Google Scholar search, for the keyword "neurofeedback"). In the following decades, the number of papers on the subject continued to grow rapidly, reaching 1,260 in the 1990s, about 6100 between 2001 and 2010, and more than 9,000 publications between 2011 and 2015, devoted to various aspects of N-EEG!

4.3.2. State of the art before starting own research

At the time I began my research (2015), reliable experimental data were surprisingly scarce, and both the methodology and the results of neurofeedback experiments were commonly inconsistent. One of the first review papers on the subject, published by Vernon (Vernon et al. 2004), looked at the use of N-EEG in the treatment of attention deficit hyperactivity disorder (ADHD). The authors discussed experimental factors such as training duration, electrode location, and signal modality, and discussed their possible influence on treatment outcomes. The paper indicated that achieving therapeutic effects requires, at a minimum, 20 N-EEG sessions and, protocols based on beta/SMR bands. However, the studies discussed by the authors raised significant concerns about the validity of this method, mainly due to the lack of control groups or evidence of training specificity related to EEG changes (Vollebregt et al. 2014; Zuberer et al. 2015).

The first quantitative review of N-EEG (Arns et al. 2009) focused on controlled studies of ADHD. This review indicated positive therapeutic effects of training. However, in contrast to Vernon (Vernon et al. 2004), Arns' team found that inattention and hyperactivity were more sensitive to non-specific factors (e.g., therapist-patient interactions) than to feedback itself. It also appeared that non-specific factors may be responsible for the training effects observed in healthy individuals (Logemann et al. 2010). Another review (May et al. 2013) conducted on patients with traumatic brain injury confirmed positive therapeutic effects of the N-EEG paradigm, but these studies lacked adequate control groups. The same methodological weakness characterized the ADHD-focused studies analyzed in the following review paper (Arns et al. 2014). Importantly, for all studies using active control groups (comparison with routine treatment with known therapeutic effects), the results of N-EEG training were negative. In the studies conducted with healthy subjects, control groups should allow for the control of the non-specific factors such as trainer-patient interactions or attentional engagement accompanying any N-EEG training. The most common and effective way is to use sham training, i.e., a procedure that includes all elements of full-fledged N-EEG training except for feedback, which is usually replaced by random generator that modifies the feedback presented to the patient. Unfortunately, this type of control has not been used in most studies performed on healthy subjects.

In conclusion, most prior experimental studies and reviews did not allow us to assess the effect of specific N-EEG experimental protocols on the relationship between EEG and the performance of the cognitive functions for which this method was used.

4.3.3. Examining efficacy of commonly used neurofeedback protocols on EEG and cognitive performance.

The literature review conducted for our planned study [1] was one of the first comprehensive assessments of N-EEG results. Its primary objective was to evaluate the efficacy of training methods in modifying electrical brain activity and enhancing cognitive performance. Additionally, we aimed to investigate the impact of commonly overlooked non-specific factors. Among several hundred publications reviewed, only 28 met the inclusion criteria due to the absence of control groups in most studies. The analysis of these qualifying studies revealed that the training methods lacked effectiveness primarily due to their low specificity, as they recorded multiple EEG bands from a limited number of electrodes.

Interestingly, the review identified consistent changes in alpha band activity across all protocols, which form the foundation of most N-EEG approaches. However, these changes were not found to be associated with the effectiveness of the training interventions. Based on our findings, we made recommendations that were positively correlated with the anticipated changes in the power of the trained EEG band(s). These recommendations emphasized the importance of training a minimal number of analyzed EEG bands while maximizing the utilization of recording electrodes.
Subsequently, our study's conclusions were validated by the research conducted by Andreas Sonderegger's group at Lausanne University of Technology (Naas et al., 2019).

4.3.4. Conducting Research on the Efficacy of Neurofeedback-EEG Training, Inspired by Recommendations Derived from Our Comprehensive Literature Review

Building upon the conclusions drawn from the literature review, we conducted our own research. Despite incorporating previously established recommendations, such as targeting attention as the specific cognitive function for training, using the beta band activity (which has documented associations with attention according to Wróbel, 2014), placing recording electrodes over regions within the frontal-parietal attentional loop, and neutralizing the impact of the trainer/therapist through rotation and employing pseudo-training in the control group, the desired behavioral and neural effects were not achieved [2]. Surprisingly, participants in the control group reported higher levels of satisfaction with the training compared to those subjected to N-EEG feedback. Although all participants were educated about the fundamental mechanisms of the N-EEG method and instructed to remain still during the experiment (with trainers intervening upon detecting excessive movement or any other undesirable behavior), nearly half of the trainees exhibited muscular activity beneath the recording electrodes, often unconsciously, in an attempt to improve their performance in the therapeutic game. As a result, the brain signals were masked by significantly higher amplitude signals originating from muscle activity [2], leading to erroneous behavioral outcomes during training.

The accumulated observations revealed that trainers were unable to effectively control and eliminate the elicitation of muscle responses, highlighting the necessity for robust online monitoring of muscle activity during N-EEG training. This requirement was particularly crucial for protocols aimed at amplifying the amplitude of higher frequency (beta) bands, as their frequency range partially overlaps with that of electrical muscle activity. Proper control of muscle activity is essential not only for obtaining high-quality EEG signals but, more importantly, for conducting genuine N-EEG training based on cerebral sources of feedback activity.

4.3.5. Investigating the Relationship between EEG Features and Cognitive performance in Laboratory and Ecological Settings

The findings from both the literature review and our own research motivated us to explore the correlations between EEG features and cognitive performance, with the aim of leveraging this knowledge for N-EEG training. We sought to identify a relationship that not only strongly correlated EEG activity with cognitive functions but also extended beyond laboratory-based psychophysiological tests to quantifiable measures in real-world ecological conditions, such as occupational or leisure activities. This approach was driven by the primary objective of N-EEG therapy, which is to enhance the daily functioning of individuals with cognitive deficits or improve performance in tasks reliant on specific cognitive functions.

In our preliminary study, we found that phase correlations of the EEG, which determine the strength of interdependence among EEG signals recorded at different electrodes, could serve as a promising parameter for exploring such relationships. Among the various available measures, we selected the phase locking value (Lachaux et al. 1999; PLV), as it is independent of spectral power and robust against motion artifacts and muscle interference (Cohen, 2015). Moreover, PLV provides a sensitive assessment of phase correlation strength, surpassing the phase lag index.

To investigate the relationship between PLV and psychophysiological tests scores, as well as behavioral outcomes related to daily activities, we employed a visual search test to evaluate attention processes and scores of shooting sports training from novice learners, which also requires significant attentional engagement **[3]**. Study involved repeated measurements of psychophysiological tests and shooting performance (points scored) administered before and after shooting training (test-retest). The results revealed that participants who exhibited higher PLV values for frontoparietal connections in the beta band (indicating stronger synchronization of brain structures) during the resting state and displayed higher global mean amplitudes of this band across all electrodes performed significantly worse in sports shooting (Figure 1A). Additionally, they exhibited weaker reconfiguration of neuronal connections (Figure 1B).

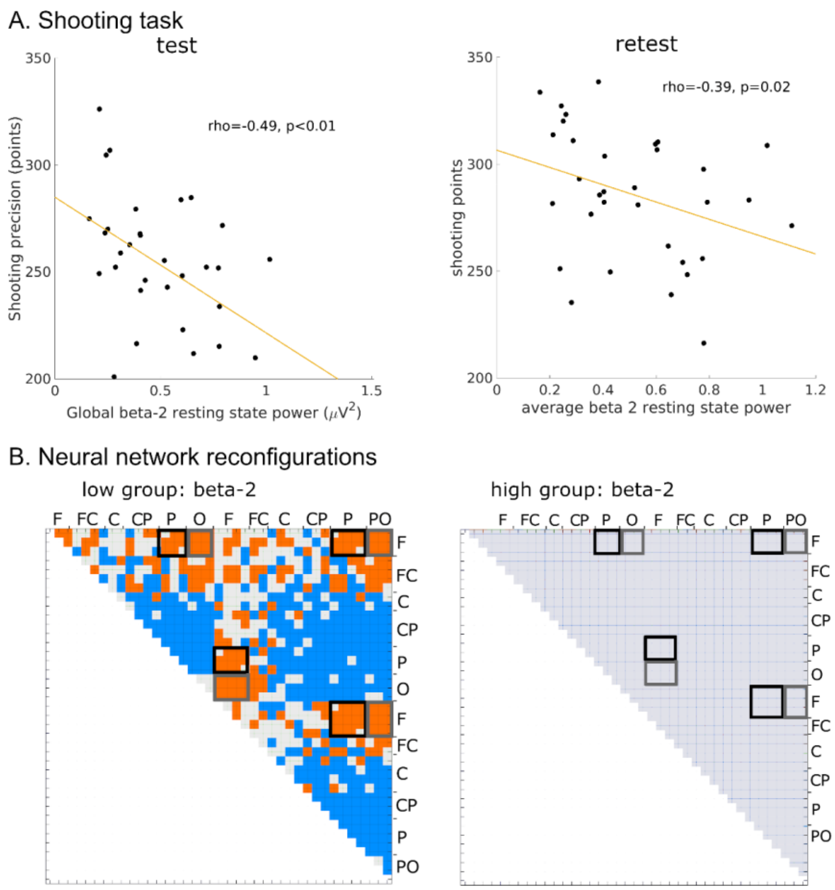

Figure 1: A. Correlations between mean global beta-2 power (22-29 Hz) during the resting state, representing the strength of frontoparietal connections in the EEG signal within this frequency band, and sports shooting performance (out of a possible 400 points). Sample size (n) = 33. B. Significant differences in the strength of EEG signal correlations ($p < 0.05$, FDR-corrected) within the beta-2 band between the retest and test sessions. The left panel displays significant differences for the group with low connection strength (characterized by low values of global mean beta-2 amplitude), while the right panel shows no significant differences for the group with high connection strength (characterized by high values of global mean amplitude). Positive differences are represented by red colors, negative differences by blue colors. Frontal-parietal connections are indicated by black outlines, while frontal-occipital connections are indicated by gray outlines. (Rogala et al. 2020)

Our findings align with earlier theoretical studies that have postulated the stability and strong connections between distant brain structures (Ermentrout and Kopell, 1990; Kopell et al., 2000; Chandrasekaran et al., 2010). These strong connections are shown to be resilient to disruption and require less energy for their maintenance (Ermentrout and Kopell, 1990; Chandrasekaran et al., 2010). Conversely, weaker phase correlations have been associated with neuronal networks of higher complexity, which exhibit greater information processing flexibility (Goldberger et al., 2002; Zappasodi et al., 2014) and improved behavioral performance (Tzagarakis, 2019). Furthermore, weaker neuronal connections facilitate network reconfiguration in response to cognitive tasks (Figure 2).

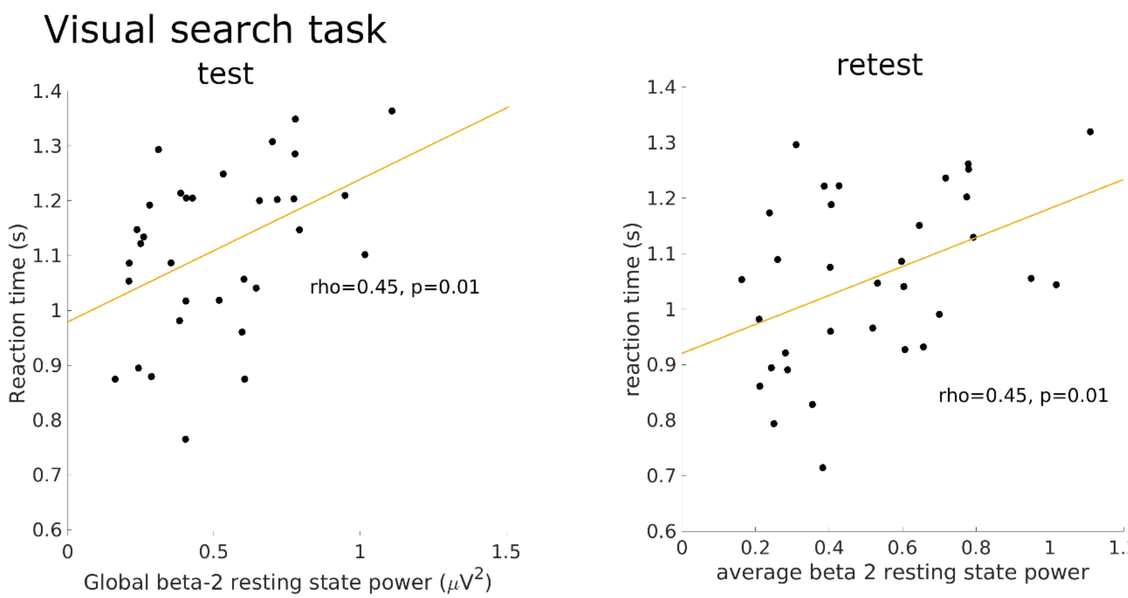

Figure 2. Correlations between mean global beta-2 power (22-29 Hz) at rest characterizing the strength of frontal-parietal connections of the EEG signal in this band and reaction times in a visual search task, n = 33. (Rogala et al. 2020)

4.3.6. Evaluating the Efficacy of Personalized N-EEG Training Parameters

Based on these findings **[3]**, a personalized experimental protocol was developed, involving the individualized selection of electrode pairs and EEG bands. The protocol preparation procedure encompassed three diagnostic sessions (Session-1, Session-2, and Session-3), with intervals of 2-3 days between each session. These sessions were designed to assess the characteristics of EEG signal phase connections during tasks that required working memory engagement.

During the diagnostic sessions, participants engaged in a computer game based on a delayed match to sample (DMTS) task using a keyboard, while a 19-channel EEG was recorded. Each session comprised randomly shuffled trials involving attention and memory demands, as well as control trials that, despite being identical, did not necessitate memory usage for accurate performance. The data acquired from the three sessions were subsequently employed to decode the EEG activity associated with correct trials that required attention and working memory engagement. The individually derived parameters were then utilized during EEG training, employing an identical game, with the training's efficacy monitored through the detection of the EEG activity state accompanying correct trials from the diagnostic sessions.

To assess the effectiveness of the training, a battery of psychophysiological tests was conducted, including the classic n-back working memory test and the transitive reasoning test, which evaluates simultaneous processing, retention, and manipulation of information—reflecting effective attention and working memory abilities. These tests were administered both before (pre-test) and after the series of N-EEG training (post-test). Additionally, in order to investigate the potential influence of previously unexplored factors related to participants' personality traits, a questionnaire measuring personality dimensions (such as extraversion and neuroticism) was completed by the subjects (Eysenck & Eysenck, 1991).

Due to the COVID-19 outbreak, the planned N-EEG experiment utilizing a protocol based on EEG phase correlations was disrupted. However, a portion of the pre-test data, which served as controls for the intended N-EEG training, was successfully collected before the lockdown. This group was subsequently referred to as the "Pre-Pandemic" in further analysis. Despite the challenges posed by the lockdown, some participants volunteered to continue their involvement in the study, constituting the "Pandemic" group. Both groups were requested to undergo psychophysiological control tests once again - the post-tests. Consequently, although the experiment could not proceed as initially intended, a unique dataset was obtained, enabling the examination of neuronal and behavioral responses to the severe and prolonged stress induced by the COVID-19 threat. This analysis was conducted among individuals with varying strengths of EEG signal phase correlations and distinct personality traits, while also comparing these results to data obtained from individuals who participated in the study prior to the pandemic [4]. Notably, the Fear of COVID-19 questionnaire completed by all participants during the lockdown period revealed no differences between the groups, indicating that the decision to continue participation during the lockdown must have stemmed from factors unrelated to fear.

Simultaneously, an analysis of the collected data demonstrated that individuals who persisted in participating during the pandemic exhibited higher levels of extraversion (Figure 3) and stronger mean global phase correlations in the EEG signal (Figure 4) in comparison to the group that concluded their participation before the pandemic.

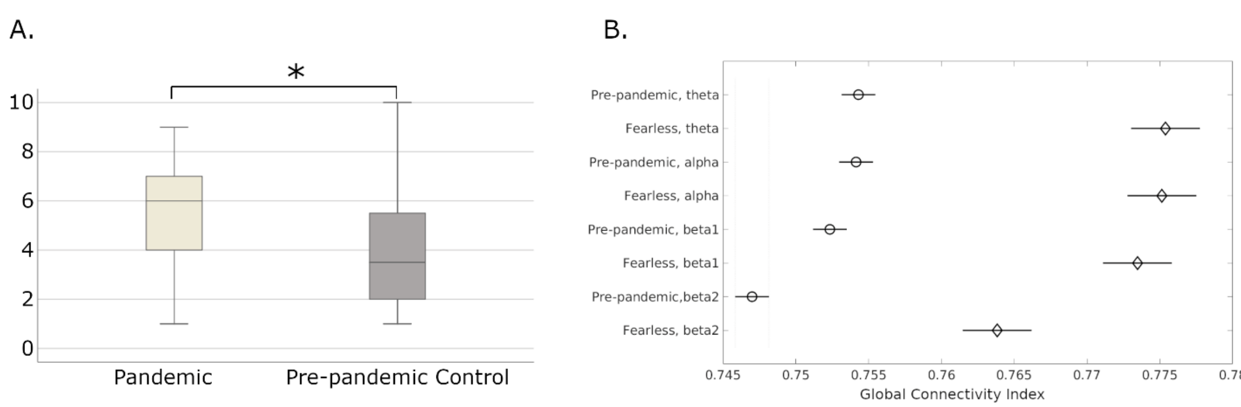

Figure 3. A. Comparison of extraversion levels on the Sten scale between the Pandemic and Pre-Pandemic Control groups during Session-1. The asterisk denotes a significant difference between the groups ($p < 0.05$, Mann-Whitney test).
B. Group average of the global connectivity index (GCI) in four EEG bands during Session-1 (pre-pandemic COVID-19).

Significant differences between the groups were observed across all bands ($p < 0.01$, ANOVA followed by Tukey's post-hoc test). GCI was calculated as the average phase locking value (PLV), a measure of connection strength based on the phase of the EEG signal, in the four canonical EEG bands: theta (4-7 Hz), alpha (8-12 Hz), beta-1 (14-20 Hz), and beta-2 (21-30 Hz). The Pandemic group refers to the participants studied during the lockdown, while the Pre-Pandemic Control group represents those who completed the study prior to the outbreak of the pandemic. (Rogala et al. 2021)

Previous studies have only touched upon the potential relationship between functional connectivity, as measured by PLV, and stress in healthy individuals (Nair et al., 2020; Alonso et al., 2015). Notably, Alonso and colleagues (2015) demonstrated that stress induced by a cognitive task resulted in an increase in beta band correlation strength. In our experiment, we also observed an increase in correlation strength across all studied EEG bands under stress, which likely stemmed from the heightened and prolonged stress associated with the pandemic threat. Participants with higher levels of extraversion were more inclined to continue with planned activities, such as their participation in the study. This finding could be attributed to the lower reconfiguration capacity of neuronal networks associated with higher phase correlation strength, consequently reducing the ability to modify behavioral responses, as described in our earlier work [3]. Interestingly, participants who did not exhibit differences in the mean global strength of connections and completed the study before the pandemic demonstrated poorer performance on repeated tests (post-test) compared to those exposed to prolonged stress (Figure 4).

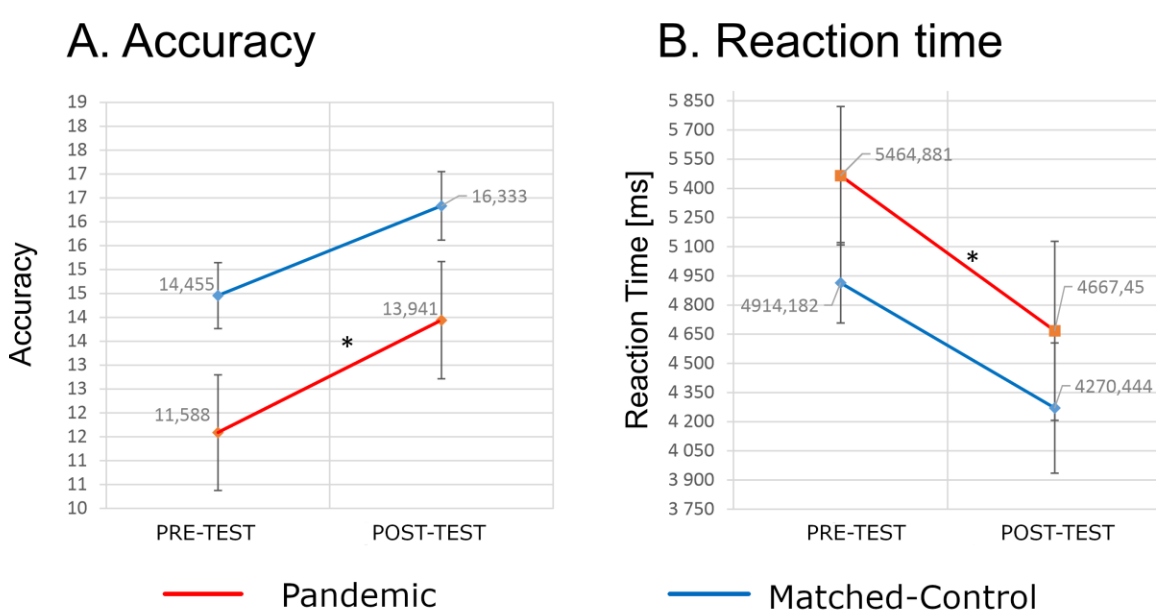

Figure 4: Accuracy and reaction time in the transitive reasoning tasks performed in pre-test and post-test. Mean accuracies in the difficult variant (A) and mean reaction times in the easy variant (B). Asterisks above the lines connecting the results of Session-1 and Session-2 indicate significant differences ($p < 0.05$) by the Chi2 post-hoc test, followed by Friedman's non-parametric ANOVA. Matched-Control group of individuals who completed pre-pandemic surveys corresponding to the study group in terms of level of extraversion and GCI (global connectivity index) in a given band. (Rogala et al. 2021)

These seemingly contradictory observations can be reconciled by considering the finding that individuals with strong correlations of EEG signals may experience difficulty in altering the configuration of their neuronal networks in the absence of strong stimulating factors. Consequently, minimal or no behavioral modifications may occur in response to environmental influences. However, for those who continued to participate in the study during the pandemic, the prolonged exposure to intense stimulation may have induced changes in functional connectivity, subsequently modifying their behavioral responses to the given task. This could explain the observed improvement in performance among this group (Figure 5) **[4]**.

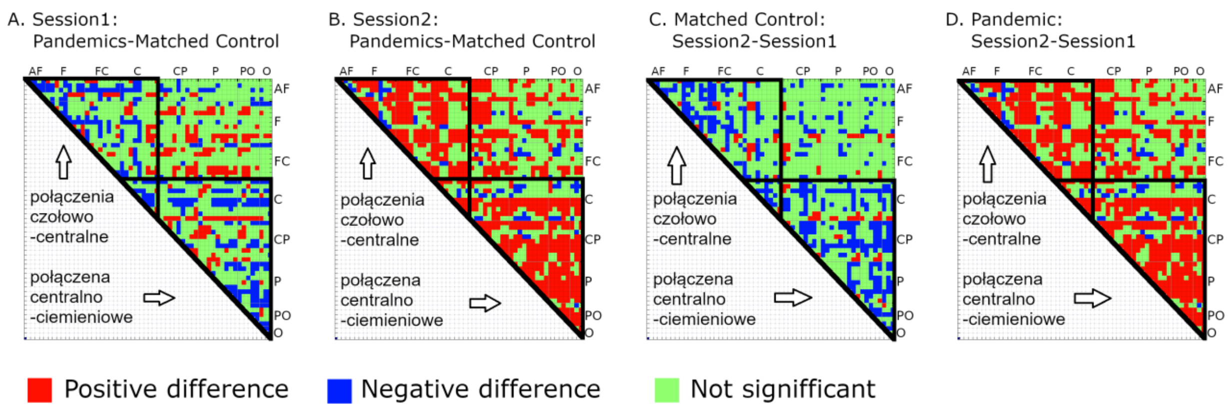

Figure 5: Comparison of PLV differences for all pairs of electrodes between the Pandemic and Matched Control groups, and between sessions for these groups, in the exemplary beta-2 band. (A) PLV differences for the Pandemic and Matched Control groups in the pre-test before the pandemic outbreak; (B) the same for the post-test, for the Matched Control group before the pandemic outbreak, and for the Pandemic group during the lockdown; (C) PLV differences between post-test and pre-test for the Matched Control group performed before the pandemic outbreak; (D) differences between post-test (collected during lockdown) and pre-test (before the pandemic outbreak) for the Pandemic group. Black contours delineate PLV differences for frontal-central and central-parietal connections. Differences significant at $p < 0.01$, after Bonferroni correction. Matched-Control group of subjects who completed the pre-pandemic study corresponding to the study group in terms of extraversion and GCI (global connectivity index) levels in a given band. Pandemic - the group studied during the lockdown, Pre-Pandemic Control - the group that completed the study before the outbreak of the pandemic. Matched-Control group of people who completed the study before the pandemic corresponding to the study group in terms of the level of extraversion and GCI (global connectivity index) in a given band. Black triangular contours outline the PLV values measured for frontal-central and central-parietal connections. Differences that were found to be statistically significant at $p < 0.01$ after Bonferroni correction are indicated. The Matched-Control group consisted of subjects who completed the pre-pandemic study and were comparable to the study group in terms of extraversion levels and GCI (global connectivity index) in the specific band. The Pandemic group refers to the participants studied during the lockdown, while the Pre-Pandemic Control group refers to the participants who completed the study before the outbreak of the pandemic. (Rogala et al. 2021)

The findings from the aforementioned studies ([3] and [4]) emphasize the importance of personalized N-EEG therapy, as both strengthening and weakening neuronal connectivity, along with other EEG signal features, can have a beneficial therapeutic effect depending on individual patient predispositions and external circumstances. However, it is worth noting that the third experiment described (**[4]**), which aimed to identify personalized parameters for N-EEG training, involved a complex and time-consuming development of a customized protocol. The requirement for individual electrodes and EEG band selection, as well as multiple comparisons of averaged

PLVs between experimental and control trials, demanded specialized knowledge, software tools, and considerable effort. These factors pose limitations to the practical application of the developed method in clinical settings. Furthermore, the binary nature of the phase correlations of the EEG used in both studies failed to capture the simultaneous interaction of signals from multiple channels, and other EEG signal characteristics such as power and functional relationships between different frequency bands were not considered in the protocol. Consequently, even with meticulous customization, a protocol may not fully deliver the expected changes in brain activity or improvements in behavioral outcomes.

In order to mitigate these challenges and enhance the process of developing individualized protocols, another study has employed artificial neural networks [5].

4.3.7. Exploring application of Artificial Neural Networks for Neurofeedback-EEG Training

Artificial neural networks, particularly deep neural networks (DNNs), have demonstrated their effectiveness in various research domains for feature extraction in end-to-end data classification. Schirrmeister et al. (2017) and others have successfully applied this approach to clinical EEG recordings. However, the practical application of DNNs for EEG classification faces two main challenges: (i) limited availability of large datasets, leading to the risk of overfitting, and (ii) lack of understanding and interpretation of relevant features used in the classification process, often referred to as the "black-box" issue. These limitations introduce the risk for using artifacts in classification, which can have negative implications for neurofeedback or diagnostic applications, resulting in false diagnoses and undesired side effects (Comstock et al. 1992; Nathan and Contreras-Vidal 2016).

The challenges associated with small dataset sizes and the need for explainability of classification results have been recognized for some time. Techniques to mitigate these issues have been developed and applied in various fields, including EEG research. To address the problem of small datasets, transfer learning has become a widely used technique since its early application in 1998 by Thrun and Pratt (1998). More recent advancements include unsupervised contrastive learning (Hyvarinen and Morioka 2016), which has shown promising results in EEG studies (Mohsenvand et al. 2020; Banville et al. 2021). Similarly, techniques like sensitivity analysis and the probability gradient method have been employed to enhance interpretability. Sensitivity analysis, in particular, is a popular method that evaluates the local gradient of the output relative to input features, providing heat maps that highlight features with the greatest impact on the output.

The prevailing trend in machine learning is often focused on achieving high accuracy at the expense of interpretability and explanation of results. However, considering the risk of artifact-based classification, it is crucial to investigate the impact of classifier types and artificial neural network training methods on the selection of features used by classifiers. Regrettably, we have not found extensive research in the literature that specifically addresses this aspect, as previous studies have primarily focused on classifying EEG activity using a single type of training and classifier (Bird et al. 2018; Chakladar et al. 2020; Han et al. 2020).

In order to investigate the impact of training type and classifier on the relevance of input features, we utilized data collected in previous studies during three diagnostic sessions **[4]**. To conduct the analysis, we developed four artificial neural network models employing two different training methods [5]. By applying different models and training methods to the same dataset, we could compare the effects of various architectures, training strategies, and input data representations on classification outcomes and the significance of individual EEG features in the classification process.

The artificial neural network models used in the experiment were as follows:

- Shallow ConvNet: a reference model originally developed by Schirrmeister et al. (2017).
- Parallel ConvNet: This model utilized an input signal representation in the form of channel-frequency-time and shared the convolutional part of the architecture with the Hybrid model.
- Hybrid model: Similar to the Parallel ConvNet, also employed the channel-frequency-time input representation. However, it was further trained to classify individual participants.
- Contrastive model with gated multilayer perceptron (gMLP-MoCo): designed to evaluate transfer learning using contrast training.

For training the Shallow ConvNet, Parallel ConvNet, and the pre-trained portion of the Hybrid model, we employed the AdamW optimizer and utilized a standard binary cross loss function. As for the gMLP-MoCo model, its training consisted of two stages: unsupervised pre-training on clinical data using momentum contrastive learning (MoCo) in the first stage, followed by training of the pre-trained network on data from the current experiment in the second stage.

The inclusion of contrastive training in our study served two purposes. Firstly, it allowed us to evaluate the impact of this type of training on the relevance of features, specifically focusing on the features of the EEG that could provide insights into the correlates of neural activity related to information retention in working memory. Contrastive learning methods, which introduce transformations of the training set to extract invariants, have been widely utilized in various fields (Wu et al., 2018; Chen et al., 2020; He et al., 2020; Tian et al., 2020). Secondly, we employed perturbation analysis with automatic probability gradient estimation to identify and assess the significance of features for classification results.

To establish a reference to commonly used traditional EEG analyses, we focused on the power of the EEG signal in the canonical frequency bands at each electrode. We used classical spectral analyses in each band as a reference for the perturbation analyses. The power in each frequency band was estimated by summing the periodograms within the frequency ranges corresponding to the Morlet wavelets utilized in our models. To determine the significance of the features, we conducted permutation tests by shuffling the labels for each electrode-frequency combination.

The classification results obtained with the employed classifiers and training methods demonstrated the highest performance for the most complex models, particularly the contrast learning-based model using the raw data, as shown in Table 1.

Table 1 Classification results for each model (Żygierewicz et al. 2022)

Model	ACC	MCC	# Trainable parameters
Shallow ConvNet	61.50 ± 2.33	0.216 ± 0.030	3.5×10^4
Parallel ConvNet	62.06 ± 1.39	0.223 ± 0.025	2.1×10^4

Hybrid model	64.38 ± 0.60	0.264 ± 0.011	2.1×10^4
gMLP-MoCo	65.29 ± 0.76	0.288 ± 0.018	6.1×10^6

The relationship between the power spectrum in the canonical EEG bands and cognitive functions has been a topic of investigation since the early days of electroencephalography. While the exact mechanisms are not fully understood, the EEG correlates of working memory have been extensively studied and are among the most well-understood phenomena. By comparing the spectral features used by our models for classification with classical spatial-frequency analysis and current knowledge, we can determine whether the classification results align with known physiological phenomena. Such correlations are of significant importance in the fields of medicine and biology.

Traditional methods of EEG analysis involve statistically comparing predefined measures recorded in selected regions of interest under different experimental conditions. In contrast, artificial neural networks utilize information from all available features and locations simultaneously, providing additional insights into the contributions of various physiological and functional mechanisms, including previously unknown ones, which are relevant to classification results.

Interestingly, all the models that exhibited high mutual similarity in terms of relevant features shared common characteristics, including shallow architectures, a relatively small number of trained parameters, and supervised learning. The most prominent features observed across these models included positive feature importance index values in the theta band (5-8 Hz) recorded on frontal electrodes, and negative feature importance index values on parietal electrodes centered around frequencies of 11 Hz (alpha) and 15 Hz (beta) (Figure 6A-C). These features have been extensively documented in psychological and neuroscience studies on EEG and working memory. It has been consistently demonstrated that storing information in memory is associated with increased power in the theta band recorded at frontal electrodes (Wilson et al., 1999; Bastiaansen et al., 2002; Klimesch et al., 2008; Michels et al., 2010; Sauseng et al., 2010). Although the physiological interpretation of other features, such as the activity of alpha and beta bands on parietal electrodes, is more challenging, these features have also been detected in numerous electrophysiological experiments (Pavlov and Kotchoubey, 2022).

In summary, the relevance of features such as theta band activity on frontal electrodes to the classification results indicates that the models studied are based on features that can be interpreted using classical electrophysiological methods. This finding strengthens the validity and interpretability of the classification results obtained from our models.

In addition to the previously described features, the probability gradients calculated for the gMLP-MoCo model with contrastive learning revealed patterns of other relevant features that had higher importance for the classification results compared to those observed in the shallow architecture models (Fig. 6D). Particularly noteworthy is the high feature importance index for the delta and theta bands at the Fp1 and Fp2 electrodes, and to a lesser extent, for the gamma band in the frontal and occipital regions. These findings suggest that the model was utilizing features associated with artifacts related to eye movements and muscle activity for classification, despite the preprocessing steps taken to remove such artifacts from the experimental data, including the elimination of electrical recordings of eye blinks and muscle activity. Additional verifications excluded possibility that high values of feature importance index on the features related to artifacts resulted from clinical training set.

These results have important implications for potential applications in N-EEG training and diagnosis. The model's high sensitivity to artifact-related features practically excludes it from medical use, as it may lead to false diagnoses and unreliable results. However, it may still find practical applications in brain-computer interface (BCI) applications where the intentional modulation of such artifacts can be harnessed for control purposes.

It is crucial to address the challenge of artifact contamination in EEG classification models, as the reliance on artifact-related features can undermine the accuracy and validity of the results. Future research should focus on developing robust preprocessing techniques and feature selection methods to minimize the impact of artifacts and improve the interpretability and reliability of the classification outcomes in both N-EEG training and diagnostic applications.

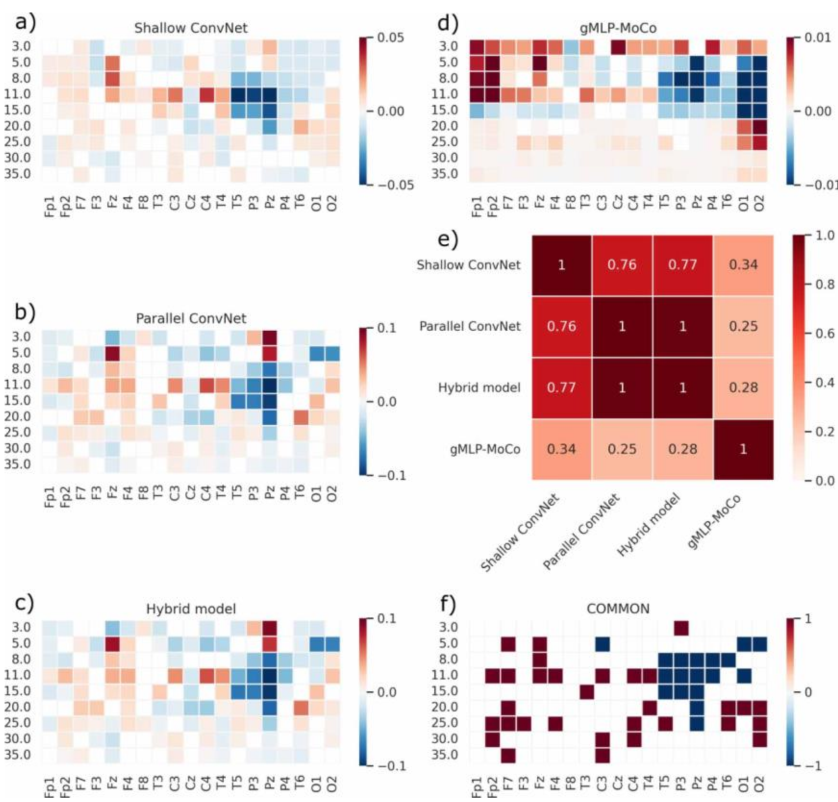

Figure 6 Results of perturbation analysis. (A-D) heat maps of the feature importance index for the four models studied. Channel-frequency pairs masked in white were not significant. (E) Spearman correlation between heat maps; all significant correlations (p<0.001) are marked. (F) Heat map elements common to all models - red positive, blue negative. (Żygierewicz et al. 2022)

To summarize the relevance of the extracted EEG signal features for classification, it is noteworthy that the shallow architecture models exhibited features that align with the physiological properties of EEG signals observed in biological and clinical experiments. The importance of these features, which have well-documented physiological relevance, confirms the validity of using artificial neural networks with shallow architectures and supervised learning to design training protocols and supervise N-EEG training.

However, it is important to acknowledge that different training methods can result in classifications

based on distinct sets of features that may not be directly related to the intended task. Therefore, when selecting classifiers and learning methods for artificial neural networks in diagnostic and therapeutic applications, it is crucial to incorporate techniques for identifying and explaining the relevance of features. This approach will help mitigate the risk of classification based on artifacts and enhance the interpretability and reliability of the obtained results.

Future advancements in the field should focus on the development of robust feature selection methods and comprehensive explanations of the significance of extracted features. By doing so, we can reduce the potential impact of artifacts, improve the accuracy of classification models, and promote the effective use of artificial neural networks in N-EEG training and diagnostic applications.

4.3.8. Summary

This comprehensive research program has allowed us to validate the effectiveness of existing methods in modulating electrical brain activity and improving cognitive function using N-EEG [1]. Our research findings revealed the limitations of previous approaches due to the lack of correlation between the utilized EEG signal features in N-EEG and the targeted cognitive functions [2]. These findings were further supported by independent experimental studies conducted by other research centers (Naas et al., 2019). The literature review [1] and our own study served as a foundation for exploring new methods that would establish a relationship between EEG activity and commonly employed cognitive tests in research laboratories, as well as activities conducted in real-world settings [2]. Additionally, we aimed to develop methods that are more resilient to experimental artifacts.

During our research, we discovered a correlation between the strength of phase correlations and the behavioral outcomes of psychophysiological test, both in laboratory settings and real-life performance [3]. Subsequent studies not only confirmed the link between phase correlations and cognitive function but also unveiled their connection with responses to severe and prolonged stress, as well as personality traits such as extraversion [4]. These findings emphasized the necessity of personalized training, involving diagnostic measurements using targeted psychophysiological tests of cognitive functions prior to actual training. They also motivated us to explore the potential of utilizing machine learning techniques in N-EEG training. Our research was pioneering in demonstrating the influence of training methods in artificial neural networks on the underlying classification features, which is crucial for personalized models in the fields of medicine and biology. Furthermore, our investigation into the application of explainable artificial neural network models for preparing and supervising N-EEG training confirmed their efficacy.

In conclusion, this research has provided valuable insights into improving the methods used in N-EEG training and their impact on cognitive enhancement. By establishing correlations between EEG, cognitive tests, stress responses, and personality traits, we have paved the way for personalized training and the integration of machine learning techniques in this domain. Moreover, our utilization of explainable artificial neural network models has contributed to the effective preparation and supervision of N-EEG training sessions.

4.3.9. References

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5. Scientific Activities

5.1. Neurofeedback-EEG

During my doctoral dissertation at the Institute of Experimental Biology, I had the privilege of collaborating with Professor Andrzej Wróbel, who was leading the Department of Neurophysiology at the M. Nencki Institute of Experimental Biology of the Polish Academy of Sciences. Professor Wróbel invited me to participate in a grant project focused on studying the mechanisms of cognitive enhancement using the N-EEG. As we began implementing the project, initial analyses revealed limited effectiveness of widely employed N-EEG paradigms. In a joint meeting with the laboratory team, we collectively conceived the idea of delving into neurofeedback methods and developing novel and more effective paradigms. Subsequently, we partnered with a prominent EEG equipment company and submitted a grant application to the National Centre for Research and Development to validate our developed paradigms. Fortunately, our application received funding, and the grant facilitated the creation of several articles discussed in this dissertation. It also led to the formulation of a patent application, in which I am listed as a co-author.

The implementation of N-EEG research through the grant provided us with an opportunity to establish a comprehensive method for objectifying and automating training procedures using machine learning techniques. The analysis of this method served as the foundation for a subsequent grant application to the Regional Funds, which also secured funding. During the grant period, I established collaborations with the Department of Physics and the Department of Mathematics and Computer Science at Jagiellonian University, as well as the Department of Physics at Warsaw University, where I am presently employed.

The research outcomes pertaining to the efficacy of N-EEG training using artificial neural networks validate the viability of this approach and are currently being prepared for publication. Psychophysiological tests conducted to verify the effectiveness of the new method, administered before and after a series of N-EEG trainings, exhibited significant improvements in the experimental group that underwent training using feedback supervised by an artificial neural network. Conversely, the control group, which underwent an identical procedure to the experimental group but with a simulated feedback mechanism generated by an algorithm independent of the participants' efforts, did not show comparable enhancements.

5.2. EEG Analysis Using Machine Learning Methods

The successful application of machine learning methods to N-EEG research motivated me to explore the application of artificial intelligence for EEG analysis in a broader context. With access to a unique and extensive longitudinal dataset obtained from resting EEG recordings during the N-EEG research, I collaborated with researchers from the Warsaw University of Technology (WUT) to investigate the efficacy of identity verification based on resting-sate EEG. Previous studies in this area relied on training artificial neural networks and validating identity using a single EEG recording divided into multiple parts. However, this approach presented several significant limitations. Firstly, a single registration does not align with the intended purpose of identity verification, which involves repeatedly verifying the identity of the same individual. Secondly, it constrains the signal variability due to factors such as differences in electrode impedance, electrode placement, and the person's emotional state. Lastly, using the same registration for both training and testing an artificial neural network can result in data leakage from the training set to the test dataset. I hypothesized that these limitations lead to an overestimation of the accuracy and sensitivity reported in previous studies.

Through research conducted on longitudinal data, I was able to demonstrate (Plucińska ... and Rogala, 2022, 2023) that tests conducted on single recording indeed overestimate classification results. Furthermore, the study determined the minimum number of EEG sessions required to achieve stable and reliable outcomes. By leveraging this longitudinal dataset, we addressed the limitations of previous approaches and obtained more accurate and robust results in identity verification using EEG. These findings have important implications for the field, shedding light on the appropriate methodology for evaluating identity verification systems based on EEG recordings. The research conducted in collaboration with WUT has paved the way for further advancements in this area, fostering a better understanding of the potential and limitations of EEG-based identity verification methods.

The subsequent advancement in utilizing machine learning methods for EEG analysis involved acquiring a license from a healthcare EEG equipment supplier to access what is arguably the largest database of clinical EEG recordings worldwide. This extensive database, consisting of over a hundred thousand recordings, is currently housed at the Center for Systemic Risk Research at the University of Warsaw (which I mention my affiliation with later in this paragraph). The primary objective of utilizing this database is to ultimately develop biomarkers for neurodegenerative changes and the aging process. To accomplish this goal, I forged a collaboration with Professor Przemyslaw Bieck from the Warsaw University of Technology. Our collaboration already resulted in second place recognition during the "W3PHIAI-23 Aging Hackathon" presentations at the 7th International Workshop on Health Intelligence (W3PHIAI-23) held at the AAAI-23 conference in Washington, DC. Aging affects organisms in diverse ways, and chronological age does not always align with biological age, as evident in conditions such as progeroid syndromes and other accelerated aging disorders. The ability to employ reliable predictors of chronological age, biological age, and their interrelationships holds significance for diagnostic and prognostic purposes (e.g., comorbidity and mortality assessments) as well as for research and clinical applications.

To secure further funding for research on biomarkers of aging and neurodegenerative changes, we submitted a grant application to the Pathfinder program within the European Horizon Europe program. For this application, I successfully formed a Consortium comprising the Warsaw University of Technology, the Technion Institute of Israel, and the University of Pisa in Italy. This Consortium represents a collaborative effort to enhance our understanding of aging-related biomarkers and neurodegenerative processes, leveraging the expertise and resources of multiple esteemed institutions. The Pathfinder grant application signifies our commitment to advancing research in this field and exploring new avenues for clinical applications.

5.3. Research on Art Perception

The exploration of art and its effects on human beings has captivated minds since ancient Greece. However, it was not until the advent of psychology as an independent discipline that the scientific investigation of art perception gained prominence. The seminal work of Fechner in 1876 marked the inclusion of aesthetics as one of the initial subjects of scientific inquiry in psychology. In more recent times, psychological research has proposed that the experience evoked by engaging with an artwork may stem from the reception of the message conveyed by the artist (Leder, 2004), where the artwork assumes the role of an information channel. This intriguing notion has prompted the utilization of information theory as a research tool to comprehend the underlying mechanisms of art's impact. The application of information theory in the study of art emerged in the 1960s, with independent contributions from Moles (1966) and Bense (1969). They respectively described artworks in terms of order and complexity, drawing from Shannon's (1948) foundational work in information theory.

The integration of information theory into the investigation of art perception has opened up new avenues for understanding the intricate relationship between art and human cognition. By employing this theoretical framework, researchers have sought to uncover the underlying principles that govern the reception and interpretation of artistic stimuli. Through the lens of information theory, art can be viewed as a means of communication, transmitting messages that elicit unique cognitive and emotional responses in viewers. This interdisciplinary approach has enriched our comprehension of the multifaceted nature of artistic experiences and deepened our appreciation for the interplay between aesthetics and psychology. Ongoing research in this field continues to shed light on the mechanisms through which art captivates and resonates with individuals, contributing to the ever-evolving tapestry of scientific knowledge surrounding art perception.

However, there remains a gap in our understanding of the complete process of information flow from the artist to the recipient, which is crucial for perceiving the artist’s intent and the associated impact of their work. While a theoretical consideration of an information encoding/decoding mechanism was proposed in a published article (Rogala et al. 2020), there is still much to explore in this area. To address this, an experiment was conducted in collaboration with the Nicolaus Copernicus University in Torun, focusing on the reception of intention encoded in abstract paintings.

The experiment consisted of two exhibitions held at a prestigious art gallery in Torun and involved two groups of participants. The first exhibition showcased abstract works by a contemporary Polish artist, while the second exhibition displayed images generated by a randomly perturbed artificial neural network the BigGAN (Generative Adversarial Network - GAN). BigGAN is capable of producing photorealistic images based on predefined categories, but in this case, the random perturbation of its weights resulted in pseudo abstract images without intentional content.

Data was collected through eye tracking, EEG, and questionnaires. The initial findings, presented at the annual Peripatetic Conference organized by the Human Interactivity and Language Laboratory at the University of Warsaw, revealed significant differences in the reception of the two exhibitions. Despite both exhibitions utilizing the same format, execution (digital printing), and visual properties of the works, the results indicated contrasting responses from the participants.

Furthermore, a collaboration with the University of Hertfordshire in the UK is currently underway to analyze the computational topology differences between the images presented at the two exhibitions. Preliminary results suggest distinct characteristics of persistence homology between the human-generated images and those generated by the perturbed artificial neural network. This analysis aims to provide further insights into the variations observed in the reception of the exhibited artworks.

Overall, this ongoing research seeks to deepen our understanding of the complex process of information transmission in art, shedding light on the role of intention and its reception by exploring the interplay between human-generated and artificially generated abstract images.

6. Organizational and Science Popularizing Achievements

6.1. Systemic Risk Research Center

The Systemic Risk Research Center (https://cbrs.uw.edu.pl), of which I am a co-founder, was established as part of the implementation of Measure I.3.2 "Initiation of a systemic risk research project" in Priority Research Area V "In search of regional solutions to global challenges ", which is part of the "Excellence Initiative - Research University" project implemented by the University of Warsaw.
The essence of the Centre's activity is to combine the perspective and reflections of the social and humanities with the wealth of data that is the domain of researchers in the field of exact and natural sciences. This stems from the conviction that in order to understand the crisis of civilization and find ways out of it, it is necessary to combine the precision of models created by exact sciences with a deep understanding of man, societies and culture typical of social sciences and the humanities. The strict approach to the study of complex systems developed by the sciences offers tools to understand the multifaceted dynamics of the crisis and integrate the perspectives of other branches of science.

Among the tasks carried out by the Center the dynamics of social and biological complex systems is a project of which I am a co-creator and contractor. The aim of this project is to adapt and use modeling methods developed by the natural sciences to understand the dynamics of complex social systems. The project includes, among other things, an analysis of aging processes. Aging of societies is one of the main systemic threats of modern civilization. Thanks to access to a large database of EEG signals of people of all ages (over 100,000 records), using advanced methods of theoretical physics, combined with the possibility of building tools and methods for classifying large databases, it is planned to develop models of aging and decay processes of complex systems that they will enable an early diagnosis of unfavorable changes, both at the level of society and at the level of individual physiology. This will enable the identification of potential compensatory mechanisms allowing for the extension of intellectual and physical performance. This project also includes the study of the mechanisms of art's impact on the central nervous system.

6.2. Innovation

Building upon my experience gained during the N-EEG study, I collaborated with a Polish company in to submit a patent application for conducting N-EEG training. The application is based on the delayed pattern matching paradigm and utilizes a multi-channel EEG transducer.

The knowledge and insights gained from this endeavor have already facilitated the development of an early marker for autism in children, in collaboration with the Institute of Mother and Child.

By analyzing recorded EEG signals, we have made significant progress in identifying potential indicators of autism.

6.3. Domestic and Foreign Cooperation

Throughout my research, I have successfully established strong collaborations with several esteemed scientific institutions, both domestically and internationally:

- Institute of Mother and Child in Warsaw: Our partnership focuses on the development of an EEG marker for autism, aiming to improve early detection and intervention strategies.
- Nicolaus Copernicus University in Toruń: Together, we conduct research on the perception of art, exploring the neural mechanisms and cognitive processes involved in aesthetic experiences.
- Warsaw University of Technology: Our collaboration centers around investigating biomarkers of aging and neurodegenerative diseases, as well as exploring the potential of using EEG signals for identity verification.
- Jagiellonian University: Our joint research efforts focus on studying art perception and utilizing machine learning methods to analyze EEG data in the context of aesthetic experiences.
- Institute of Experimental Biology them. M. Nencki: Our collaboration involves studying changes in EEG signals induced by strokes, aiming to improve our understanding of brain activity and potential recovery mechanisms.
- University of Hertfordshire: Together, we explore the computational topology of artistic images, investigating the application of mathematical and computational methods to analyze and understand visual art.

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