01
BrainT19-0051
Poster Presentations - March 4-5 - Exhibition Hours

Neurowellness

Naturalistic virtual reality Platform for studying human behavior and neurophysiology

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Background

Virtual reality (VR) has the potential of "bringing the best of both worlds" – retaining the advantages of controlled laboratory experiments, while approximating the real world in ecological validity. We have developed a methodology and a technical platform that allows placing a participant within rich scenarios, logging scenario events, neurophysiological and behavioral data. A highly automated system processes each signal and then provides generic scripts for joint data analysis and machine learning.

Results

Our framework is now being used in two experiments, selected to capture intense scenarios from student life: flirting with a stranger in a bar, and going through a job interview. We log the following data streams: skin conductance, heart rate and its derivatives, respiration, head movements, and voice. Each stream is processed separately with tools such as Ledalab, biosig, EEGLab, text2vec "deep learning" analysis of natural language, combined with in-house software. Head motions required in VR experiences present a specific challenge to all brain imaging methods, which require a stationary head to avoid artifacts.

In one type of analysis the participants provide moment to moment reporting of their subjective state (e.g., stress) using a VR controller, either during the experience or in a post viewing session. This time series is then used as a target for machine learning applied to features extracted from the various neurophysiological signals. Additionally, the platform supports event related analysis of neurophysiological signals locked to specific events in the VR.

Conclusions

The platform can be used to study human behavior and neurophysiology in simulations of arbitrary situations, including situations that are not possible in reality. Our current focus is on measuring ``stress'' as a first step towards developing future protocols for intelligent stress monitoring and regulating technologies.

02

BrainT19-0044
Poster Presentations - March 4-5 - Exhibition Hours

Neurowellness

MENTALIZING-BASED INTERVENTION FOR STRESS REGULATION

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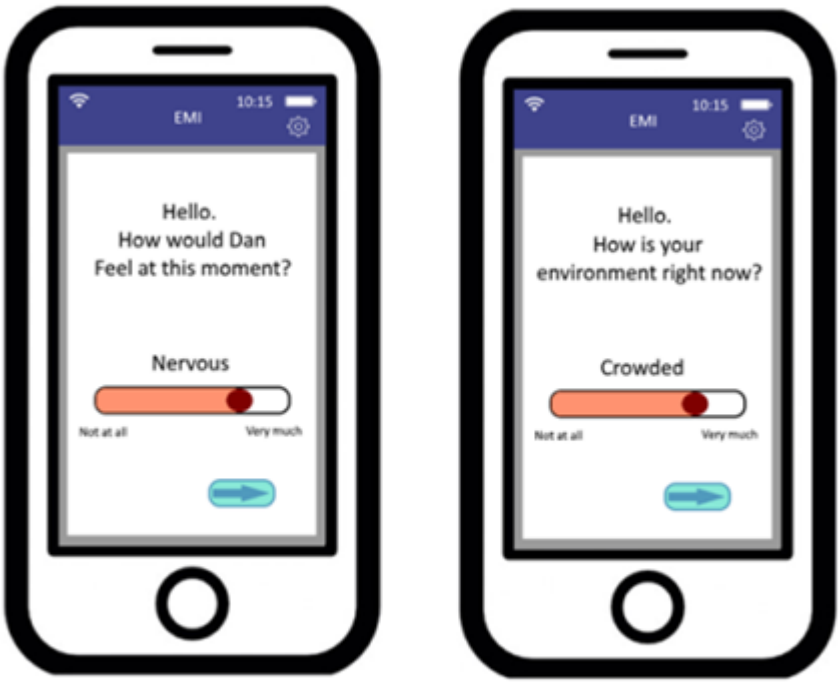
Emotion regulation (ER) plays a significant role in well-being. The most researched ER strategies, reappraisal and distraction, require cognitive control and are dependent on the presence of an emotional event. We wish to develop an ER intervention, based on people's natural capability to **Mentalize** - to understand and empathize with the experiences of others. Mentalizing relies on different brain circuits than those involved in cognitive control and is independent of external stimuli. In Stage 1, we examined the efficacy of Mentalizing-based ER in the context of social stress. Results using physiological data suggested that Mentalizing may work to up or down regulate negative emotions when the perspective-taker's resilience level is relatively close to that of the model. In Stage 2, we compared different variants of the Mentalizing intervention, in order to optimize its efficacy. Results from two studies with large samples showed that participants in the Mentalizing conditions reported significantly lower levels of negative affect than controls. Mentalizing was most effective when the model was a similar distant other, who is more resilient but not by much, to the subject. In Stage 3, we will explore whether Mentalizing-based ER can be used to reduce stress throughout people's daily lives, by using Ecological Momentary Intervention (Figure 1). This project could set the stage for the development of a smartphone application for the promotion of affective regulation.



a. Mentalizing condition **b. Control condition**

03
BrainT19-0043
Poster Presentations - March 4-5 - Exhibition Hours

Neurowellness

Increased reliability of physiological interoceptive signals following a mindfulness intervention is associated with adaptive emotion regulation choices.

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Burgeoning research on mindfulness suggests that it has widespread beneficial effects on wellbeing, resilience and mental health. Still, the mechanisms underlying the beneficial effects of the practice remain vague. In search of these mechanisms, we demonstrated that Emotion Regulation Flexibility (ERF) - the ability to use different emotion regulation strategies in accordance with changing situational demands, which is believed to underlie mental health - increased following an 8-week mindfulness course. Central to mindfulness practice is the systematic cultivation of body awareness and sustained attention towards bodily sensations. Thus we hypothesized that increasing the reliability of interoceptive signals - defined as afferent information arising from within the body - through such training supports the ability to make better choices of emotion regulation strategies.

To test our hypothesis, N=80 individuals were randomly assigned to a mindfulness intervention or to a wait-list control. Before and after the mindfulness workshop, we assessed explicit interoception through the Heart-Beat Detection task and implicit interoception through peripheral physiological signals which were measured during the ERF Task.

Our findings support our hypothesis: mindfulness practice increased explicit interoceptive abilities as well as self-reports of well-being. Pre intervention, there was no difference between groups in ERF patterns and peripheral physiology was not related to regulatory choices. Post intervention, only in the mindfulness group, ERF patterns changed and heart-rate deceleration rates and EMG activity were associated with ER choices. Our findings suggest increased reliability of interoception abilities following mindfulness, which can support more beneficial choices, including emotional regulatory ones. Our findings will be discussed in the framework of the predictive-coding models and in their possible implications to mental health, resilience and well-being.

04
BrainT19-0048
Poster Presentations - March 4-5 - Exhibition Hours

Neurowellness

Can machine learning approaches lead us toward personalized cognitive training?

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Cognitive training efficacy is controversial. Although many recent studies indicate that cognitive training shows merit, others fail to demonstrate its efficacy. Different types of cognitive trainings have been extensively investigated. These inconsistent findings may partly be the result of the high variance between studies or from differences in individuals' ability to benefit from cognitive training in general, and from specific training types in particular. Consistent with the move toward personalized medicine, we plan to use machine learning approaches to produce predictions that will help us optimize cognitive training gains. For that aim, we reached out to different laboratories across the globe asking them to share their cognitive training studies data sets with us. Thanks to the positive response we were able to collect training data of almost two thousand adult participants. All of the collected data sets were already published, consisted of an emotional pre and post training standardized measurements and trained cognitive functions. Main training types included working memory training, attention bias modification, cognitive bias modification and inhibitory control. A systematic review of these data sets will be presented and discussed. This systematic review highlight the necessity of advance analysis in the context of cognitive training and points to future research avenues.

05
BrainT19-0047
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

Abnormal Functional Frontal Asymmetry and Behavioral Correlates in Adult ADHD: A TMS-EEG Study

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Background: Abnormal functional brain asymmetry and deficient response inhibition have been implicated as central to attention deficit hyperactivity disorder (ADHD). **Objective:** To investigate the relations between brain asymmetry abnormalities and response inhibition deficits in adults with ADHD and whether altered frontal excitability and/or compromised interhemispheric connectivity may mediate frontal asymmetry abnormalities in this disorder.

Methods: Frontal asymmetry of the stop-signal N200 event-related potential (ERP) component— which is lateralized to the right hemisphere and related to response inhibition— was compared between groups of 52 ADHD and 43 non-clinical adults. We additionally examined group differences in (1) response inhibition performance; (2) TMS-evoked potential (TEP) in the right frontal hemisphere— indicative of local cortical excitability; and (3) frontal right-to-left interhemispheric signal propagation (ISP)— reversely indicative of interhemispheric connectivity. Relations between N200 frontal-asymmetry and these measures were also examined.

Results: The ADHD group demonstrated reduced N200 right-frontal-asymmetry, weaker TEP and stronger ISP than that of controls. Moreover, N200 right-frontal-asymmetry was positively correlated with response inhibition performance and with TEP in the ADHD group, while no similar relation was observed for ISP.

Conclusions: Abnormal frontal asymmetry is related to a key cognitive deficit in ADHD and may be subserved by reduced right-frontal excitability.

06
BrainT19-0028
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

MODULATING SCAR COHERENCE BY CULTIVATING INJURED NERVOUS TISSUE ON SURFACE-ENGINEERED CORALLINE SCAFFOLDS

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INTRODUCTION: Biological scaffolds provide a supportive environment for tissue generation and may be strong candidates for repairing damage in the nervous system. Scaffolds made of coral skeletons promote bone regeneration and provide nutritional support for neurons *in vitro*. This study characterizes the structural reaction of an injured nerve tissue to contact with coralline scaffolds of distinct topologies, as a prerequisite test of its usage for nervous tissue repair *in vivo*.

METHODS: Hippocampal slices from postnatal rats were cultivated on two distinct shaped of coralline scaffolds: 1. Micro-rough surface, porous, complex 3D architecture - made of intact skeleton pieces (ISP); 2. Macro-rough surface, non-porous, planar - a powder-like scaffold made of grained skeleton (GS). Visualization of the samples was done by scanning electron microscope to identify tissue-scaffold interactions and confocal-fluorescent microscope to test cellular responses after performing immunofluorescence staining to specific neural markers. Characterization of the scaffold's topology and analysis of tissue micrographs were done using ImageJ software.

RESULTS: Slices strongly adhered to the surface on both scaffolds. On ISP, slices deformed into complex 3D structures by engulfing the outer surface of the scaffold without penetrating the pores, yet, preserving their coherence. By contrast, on GS, slices were planar but broken into interconnected small segments of tissue, depending on the grains' size and density . Both scaffolds induced formation of reactive astrocytes however, whereas on GS these cells tightened into a single thin stripe at the slice's periphery, on ISP, they dispersed globally, forming meshes having inter-cell distances spanning up to dozens of microns.

DISCUSSION & CONCLUSIONS: The results demonstrate that implantation of scaffolds of pre-designed roughness and porosity can provide a control over the coherence and shape of nerve and scar tissues in the site of injury, opening a route for cell invasion, thus assisting in damage repair following brain wounds.

07
BrainT19-0021
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

Regulation of Astrocytic Reactivity and Scar Formation by Coral Skeleton in a Novel in-vitro TBI Model

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Traumatic brain injury (TBI) results in massive cell death and scar-tissue formation, disabling self-recovery. Reducing scar formation by grafting scaffolds may be a promising strategy to evoke recovery. Previous studies in our lab demonstrated positive effects of nurturing coral skeleton scaffolds on astrocytic survival and activation in-vitro. This study aimed to develop an in-vitro injury model, where the scar formation-related processes could be evaluated. In this model, the injury, treatment and astrocytic reaction were presented as follows: 1. Injured tissue: a 0.7X0.7X1mm hippocampal tissue slice, injured at all edges. 2. Scaffold implantation: Presented by cultivation of the injured slice on coral-skeleton matrices. 3. Scaffold manipulation for regulation of scar formation: Two scaffold surfaces were designed: (a) intact skeleton piece (ISP): porous, microrough; (b) grained skeleton (GS): nonporous, macrorough. 4. Astrocytic reactivity: presented as acquisition of spiky shape and overexpression of GFAP in astrocytes within the slice and among astrocytes migrating out of the injured tissue. 5. Scar formation: observed as assembly of these astrocytes into large dense structures. The results showed that on GS, the tissue exhibited a scar-like organization at its periphery and astrocytes migrating out of the slice dispersed evenly. On ISP, there was no scar-like organization within the slice, nor among migrating cells. On GS, but not on ISP, the morphology of the migrating cells changed gradually, from spiky (near the tissue) towards flat (at the culture's edge). In terms of GFAP levels, an expression gradient was detected among migrating astrocytes, from low to high levels near and far from the slice (respectively). Total GFAP expression levels were increased on ISP, compared to GS. Altogether, these results indicate that astrocytic reactivity and scar formation can be regulated by implanting coralline scaffolds of distinct surface-architectures to TBI wounds. Such regulation may gain control over damage repair following TBI.

08
BrainT19-0035
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

Induction of EEG memory pattern in hippocampal formation by transcutaneous vagus nerve stimulation - in vivo studies

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AIM OF THE STUDY The aim of the study is to investigate the impact of t-VNS on electrical patterns of theta rhythm recorded from hippocampal formation.

METHODS In studies Wistar rats were used. A tungsten electrode wire (0.1-0.9 MΩ) for recording hippocampal field activity was placed in the right dorsal HPC, in the stratum lacunosum-moleculare. Two uninsulated tungsten electrodes (0.1-0.2 kΩ) were used for bipolar VNS through the left lobule of the auricle. Three different points of stimulation were tested and following VNS intensities were tested: 0.2, 1, 2, 4, 6, 8 and 10 mA with the frequency range 5-60 Hz. The remaining parameters were constant: pulse duration (1 ms) and train duration (10s).

RESULTS The entrance of the auricular lobule was found to be the most effective in inducing theta rhythm after transcutaneous stimulation of vagal nerve endings. This effectiveness is determined by its intensity. To obtain indirect effect of t-VNS on hippocampal formation theta rhythm it is necessary to apply electrical pulses in intensity from 6mA to 10mA if the pulses are delivered with the frequency of 5-10Hz and pulses in the intensity range from 8-10mA if they are applied with frequency of 60Hz. T-VNS applied with pulses in the frequency 5 and 10Hz are more efficient in inducing hippocampal formation theta rhythm than t-VNS applied in the frequency of 60Hz. Repeated electrical stimulation of the vagal ending of the lobule of the auricle gives opportunity to observe a delayed effect.

CONCLUSIONS Electrical stimulation of the vagal endings of the lobule of the auricle gives opportunity to observe both direct and delayed effect on hippocampal field activity. The final effect of t-VNS depends on many factors. **Induction effect of t-VNS on theta rhythm may be a crucial solution for stimulate memory pattern in different neurodegenerative diseases including Alzheimer's disease.**

09
BrainT19-0041
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

Evaluation of transcutaneous vagus nerve stimulation on the activity of various brain structures by fMRI in human as a potential tool for memory deficit treatment.

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AIM OF THE STUDY

1. Evaluation of t-VNS non-invasive stimulation via auricular branch on limbic structure activity in healthy volunteers
2. Identification and prepare a solution of technical problems regarding electrical stimulation of transcutaneous VNS (t-VNS) during fMRI trials.

METHODS

Healthy volunteers (30 - 65 yr) undergo standard fMRI head examination procedures using 3T, Panasonic MR scanner.

Stimulation was provided by noninvasive pulse generator located outside of MRI room. Ag/AgCl electrodes (10mm) were attached to the left ear in the region of cymba concha (active and passive). Each single electrode was connected with 5 m shielded cooper wire to the pulse generator and non-inductance of wires verified. Applied stimulation paradigm of low current pulses (0.4-0.8 mA), proven to have an positive impact on cognitive processes improvement.

RESULTS AND CONCLUSIONS

We established reliable paradigm allowing to conduct repeatable fMRI trials to access impact of t-VNS on limbic structures. The most common technical problems as e.i. high resistance of skin, electrical stimulation outside the Faraday cage and connected the cable screen to Faraday cage for noise reduction were solved. Beside that, we observed direct and correlated response of limbic structures associated with learning and memory processes to low current electrical stimulation of vagus nerve.

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BrainT19-0014
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

The influence of psychotherapeutic support for families of patients with dementia of the Alzheimer's type

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Objective: Evaluation of the effectiveness of psychotherapeutic support for families of patients with dementia of the type Alzheimer's

Patients and methods. 102 families with patient suffered Alzheimer's dementia were examined (F.00 dementia in Alzheimer's disease, F.01-vascular dementia), 55 of whom was the main group, 45 - control group. In the main group there patients were treated by medicine (donepezil 5-10 mg or rivastigmine 1,5 – 3mg) and these families participate in the psychotherapy and psycho-social program, in the control group patients were carried out only by standard treatment for patients with dementia.

Results. We determined the positive effect of psychotherapeutic intervention on the quality of life of both the patient and his or her family. In main group psychosocial interventions improve and maintain patients cognitive functioning, adaptive behavior and quality of social functioning. A psychosocial correction program has been developed for such patients and their families.

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BrainT19-0037
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

PHASE-SPECIFIC INTRA-CORTICAL-MICRO-STIMULATION IN A BRAIN MACHINE INTERFACE ENVIRONMENT MODIFIES MOTOR CORTEX BETA OSCILLATIONS AND AFFECTS BEHAVIOR

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It is widely accepted that beta-band oscillatory activity, prevalent in the motor cortex, plays an important role in complex tasks such as planning and execution of sensorimotor behavior. Thus, being able to modulate these neuronal patterns in behaving animals may impact our understanding of cortical dynamics. In order to experimentally manipulate oscillations, we trained monkeys, implanted with arrays of 96 electrodes in the motor cortex, to volitionally enhance local field potential (LFP) beta-band (20-30Hz) activity at selected sites by neural operant conditioning, using a real time brain machine interface (BMI) platform. Subsequently, we applied Intra-Cortical-Micro-Stimulation (ICMS), precisely timed to oscillation phases.

We demonstrate that beta oscillations increased dramatically following the BMI training, and that their pre-movement power was positively correlated with the reaction times, and negatively correlated with task performance (success rate). Furthermore, we show that phase-specific ICMS modulated the power and phase of the oscillations, shifting local networks between oscillatory and non-oscillatory states. Lastly, these stimuli induced phase-dependent effects on the animal's behavior.

Our findings may contribute to unraveling the functional role of cortical oscillations. In addition, this research can pave the way for the use of an advanced BMI platform for a wide range of neurological and psychiatric disorders where volitional control (biofeedback) aided by fine-tuned electrical stimulations can restore normal activity whenever abnormal patterns are identified.

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BrainT19-0013
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

MODULATING CEREBRAL BLOOD FLOW AND BRAIN PLASTICITY USING REAL-TIME ADAPTATION OF STREAMING AUDIO-VISUAL CONTENT

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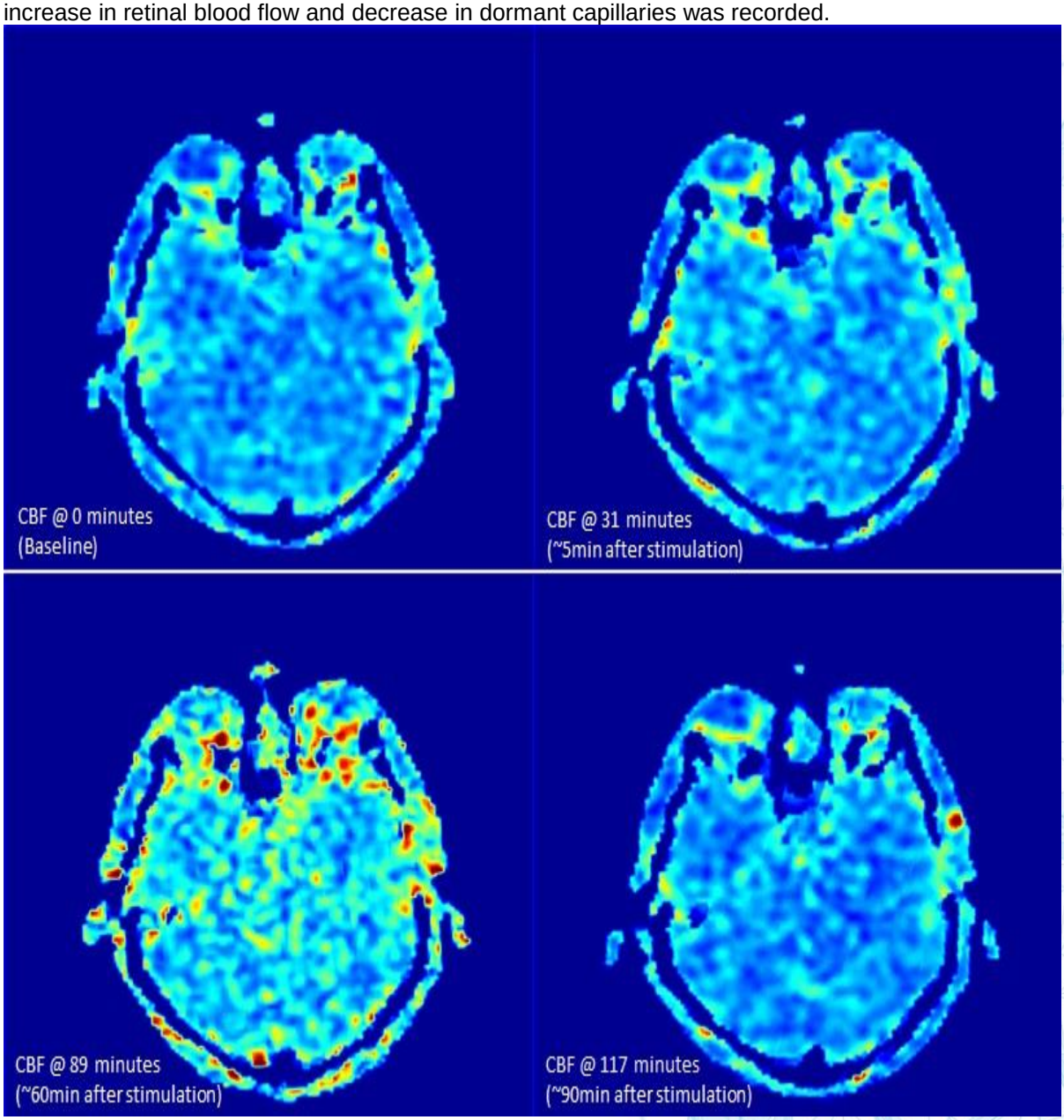
Visior introduces a video carried non-invasive delivery of visual and auditory stimulation, via respective pathways, for inducing changes in cerebral blood flow, brain perfusion, retinal blood flow, retinal perfusion and reconstruction of neural connectivity in the visual system. The stimulation is intended to enable new treatment modalities, addressing personalizing and compliance challenges via unlimited content that may be used as the stimulation carrier. A near-eye video headset, presents real-time modulated streaming content, according to a proprietary regimen, integrated in real-time, with any streaming audio-visual content. Thus, uniquely, deep brain stimulation effect is achieved via organic sensory pathways, triggering the brains auto-regulation mechanisms. Safety and efficacy of the technology was evaluated in two clinical studies and additional pilot experimenting. Brain Plasticity in the Visual Pathways was established in Amblyopia patients (a cortical vision impermeant), 27 subjects controlled clinical study at the Tel Aviv Medical Center, demonstrated average 2.2 lines (±0.158) (P=0.0002) improvement in visual acuity in just 4 weeks of home use, 2.9 lines (±0.163) (P=0.0002) after 8 weeks. No improvement demonstrated after 4 weeks in a Sham group. A Visual Pathways Signal Transfer test arm of the study, using a Visually Evoked Potentials, demonstrated up to 125% change in neural signal transfer latency and amplitude after 4 weeks of use. Cerebral Blood Flow and Brain Perfusion modulation was demonstrated in case study brain imaging pilot, using ASL MRI at the Sheba Advanced Technologies Center. Findings indicate up to 25% change in CBF and perfusion in various brain areas, after watching a 20min TV show, additional informal experimenting are in line with these the finding. Ocular Blood flow Modulation in Glaucoma patients at Indiana University US, supplements the aforesaid when immediate, statistically significant ($p < 0.0001$),

increase in retinal blood flow and decrease in dormant capillaries was recorded.



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BrainT19-0015
Poster Presentations - March 4-5 - Exhibition Hours

Brain Stimulation / Neuromodulation

Implantation of coralline scaffolds enhances nervous tissue restoration following traumatic brain injury

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Traumatic brain injury (TBI) is a major cause of mortality/disability worldwide and has no cure. The limited brain's capacity to regenerate urges identifying tissue engineering-based means to enhance histological and functional recovery. One promising strategy is grafting scaffolds that enhance cell invasion into the wound. The aragonite skeletons of corals are useful scaffolds for testing this strategy, being supportive for neural cells in culture. A quantitative penetrating TBI (QpTBI) model developed in our lab was used to perform injuries in 2 months-old mice. A precise volume of cortical tissue (2mm^3) at specific coordinates was removed by a stereotactic system-attached microdrill. Coral skeleton grains (<40µm) were mixed with collagen and polymerized to get coralline-collagen-based hydrogels, which were implanted into the wound. Implanted mice's cognitive functionality and anxiety levels were evaluated two weeks/one-month post-implantation by Morris Water Maze (MWM) and Open Field (OF) tests, respectively. Next, mice were sacrificed and thick sections containing the wound area were stained immunohistochemically to specific neural markers. Tissue micrographs were prepared using confocal microscopy and analysed by ImageJ software. We found that implantation of coralline-based scaffolds into cortical wounds induced in mice, caused histological and functional recoveries. Two weeks to one month following implantation, wounds were filled with cells in their open void volume, around and within the implants. Implanted wounds, by contrast to non-implanted, contained astrocytes, neuronal processes and precursors. OF showed that among implanted mice, walking velocity and time spent in the field's center were two-folds higher, suggesting a reduction in TBI-generated anxiety. MWM showed shorter distance/time-spent till finding the platform among implanted mice, indicating an improvement in memory skills. The results demonstrate that using coralline-based scaffolds to repair TBI has great therapeutic potential. In view of this, such scaffolds may be found helpful on other types of brain damages, such as neuro-degenerative disorders.

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BrainT19-0007
Poster Presentations - March 4-5 - Exhibition Hours

Computational Brain and Neuroscience-Inspired Artificial Intelligence

HIERARCHICAL RECURRENT CONVOLUTIONAL DEEP LEARNING NETWORK FOR DECODING EEG ACTIVITY TO PREDICT CONSUMER PREFERENCES

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There is increasing demand within consumer-neuroscience (or neuromarketing) for objective neural measures to quantify consumers' preferences and predict responses to marketing campaigns within individuals and the general population. However, the properties of EEG datasets raise various difficulties in performing predictions on them, such as small data sets, very high dimensionality, the need for elaborate and exploratory feature extraction, intrinsic noise and obscurity, and unpredictable between-subject variations. Our aim is to try and overcome these limitations using a Deep Learning Network, which have revolutionized many research fields, by combining several state-of-the-art techniques to address these drawbacks while providing interpretable results for neuroscientific insight.

In our study, we apply a DLN model to predict subject-specific value preferences based on their EEG data. In each trial, 40 subjects were presented with a product's image (out of 72 possible products) together with its short description, followed by a standard BDM task to elicit their willingness to pay (WTP) for the product. The DLN uses EEG data from product observation to predict the corresponding reported WTP values. Our novel DLN architecture considers the unique characteristics of the EEG signal by including depth-wise separable convolution for spectral and spatial filtering, and Hierarchical LSTMs for time-dependencies (within and between trials). Our interim results show 78.7% accuracy in predicting high vs low WTP, while network visualizations provide predictive frequencies and their scalp distributions, shedding light on the neural mechanism involved. We conclude that DLNs may be the superior method to perform EEG-based predictions, due to ability to consider multiple dependencies, improve SNR, and eliminate manual feature extraction by automatically identifying optimal value-related information, to the benefit of decision-making researchers and marketing practitioners alike.

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BrainT19-0034
Poster Presentations - March 4-5 - Exhibition Hours

Computational Brain and Neuroscience-Inspired Artificial Intelligence

FROM A DEEP LEARNING MODEL BACK TO THE BRAIN - INFERRING MORPHOLOGICAL MARKERS AND THEIR RELATION TO AGING

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Deep convolutional neural networks (CNN) enabled a major leap in image processing tasks and were recently applied to brain imaging data. This approach provides high predictive power, however it is often difficult to identify the features that underlie a given prediction, hence these findings are regarded as 'black box' solutions that are difficult to interpret. Discovering which features, or in the current research, brain structures, contribute most to the prediction of subjects' specific information have significant theoretical and translational value. Previous work examined methods to attribute pixel or voxel-wise contribution to the prediction in a single image, resulting in 'attribution' maps that were found noisy and unreliable. Here, we developed a novel inference framework for combining these maps across subjects, which allow us to achieve a more coherent, reliable measure of the significance and contribution of different anatomical regions to the model's prediction. We demonstrate this method using a CNN trained on predicting subjects' age from anatomical T1 brain images of ~11,000 healthy subjects with known age that were obtained from various open-source datasets. We focus on normal aging considering its widespread effects on brain structure and function. Evaluating the model on an untouched test (n = 380) resulted with MAE of 4.79 years and a correlation between the real age and predicted age of r=0.96. Applying the inference method, we were able to relate relevance score to specific anatomical structures. The highest score was assigned to parts of the basal ganglia and the cingulate cortex, both presented significant age-related volumetric decline in previous studies. We provide a framework for utilizing basic population statistics on a collection of 'attribution maps' obtained from a large group of participants. Future development of this approach could enable gaining insights from models previously considered a 'black box' and utilize them to create novel predictions.

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BrainT19-0032
Poster Presentations - March 4-5 - Exhibition Hours

Computational Brain and Neuroscience-Inspired Artificial Intelligence

Input dependent encoding of basal ganglia neurons

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The basal ganglia (BG) have an important role in the processing of motor, cognitive and limbic information through their reciprocal connections with the cortex. Abnormal BG activity has been related to a variety of sever disorders, including Parkinson's disease. Characterizing the computational properties of individual BG neurons is crucial for understanding their contribution to normal brain function and its breakdown during different pathologies.

We used a generalized linear model (GLM) to quantify the encoding of individual neurons by incorporating a linear stimulus filter, a spike history filter, and a bias term. The model was generated by fitting parameters to the in-vitro whole-cell responses of the neurons to repeated stimulation. These models accurately reproduced the responses of the experimentally recorded cells, however, the GLM parameters were found to be highly sensitive to the internal state of the neurons, such as the dependency on the baseline firing rates. Moreover, the GLMs were not inter-exchangeable, such that there was no single GLM of a neuron that was useful for all of its states. This indicates that the underlying computation of the neuron is not independent of its firing rate, and that there is no single "real" encoding of a neuron, but rather an input dependent encoding. We show how different encoding properties are dependent on the baseline firing rate, and their influence on the information processing and the fidelity of the neuron.

As the firing rate of real neurons typically fluctuates over multiple time scales, this finding is crucial for understanding the principles of information transmission, which are dynamic and are dependent on the state of the network. We propose that this input dependent computation contribute to the deficient in computational capabilities of BG neurons during Parkinson's disease, due to the change in firing rates throughout the BG over the course of the disease.

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BrainT19-0027
Poster Presentations - March 4-5 - Exhibition Hours

Computational Brain and Neuroscience-Inspired Artificial Intelligence

Decoding Visual Representations of Objects from Brain Data during Object-Grasping Task with a BMI controlled Robotic Arm

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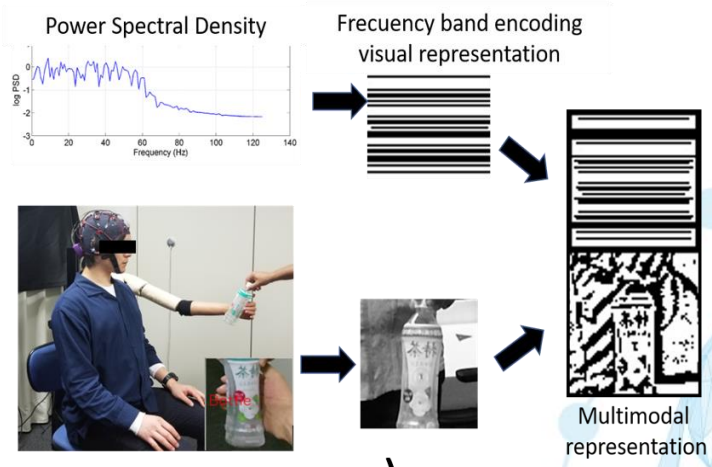
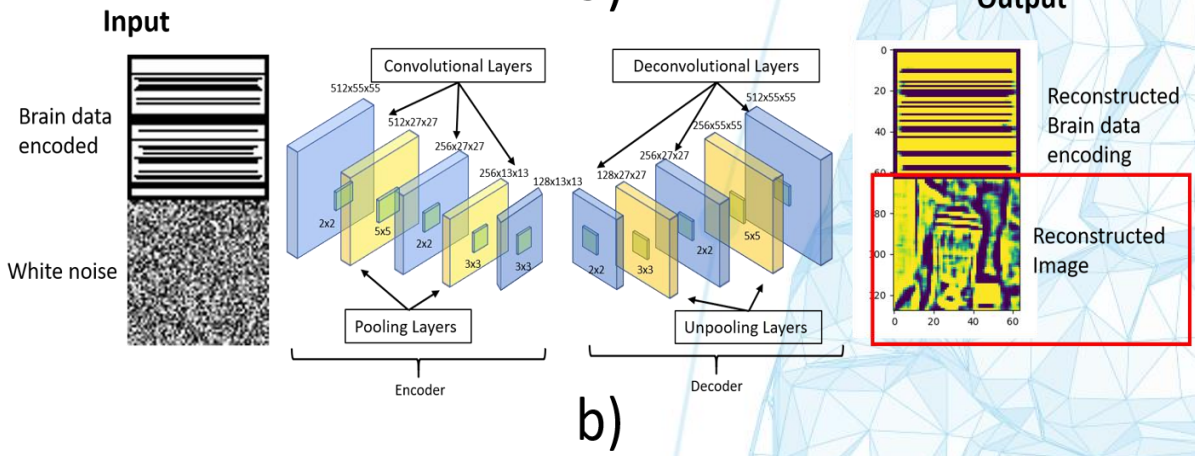
Brain-machine interface systems (BMI) have allowed the control of prosthetic and robotic arms using brainwaves alone to do simple tasks such as grasping an object, but the low throughput information of brain-data decoding does not allow the robotic arm to achieve multiple grasp configurations. On the other hand, computer vision researchers have mostly solved the problem of robot arm configuration for object-grasping given visual object recognition. It is then natural to think that if we could decode from brain data the image of the object that the user intends to grasp, then the robotic arm could automatically decide the type of grasping to execute. For this reason, in this paper, we propose a method to decode visual representations of the objects from brain data towards improving robot arm grasp configurations. More specifically, we recorded EEG data during an object-grasping experiment in which participants had to control a robotic arm using a BMI to grasp an object. We also recorded images of the object and developed a multi modal representation of the encoded brain data and object image, as shown in fig. 1a.

Given this multi modal representation, the objective was to reconstruct the image given that only half of the image (the brain data encoding) was provided. To achieve this goal, we developed a deep stacked convolutional autoencoder that learned a noise-free joint manifold of brain data encoding and the object image. After training, the autoencoder was able to reconstruct the missing part of the object image given that only brain data encoding was provided, as shown in figure 1b.

Performance analysis was conducted using a convolutional neural network (CNN) trained with the original object images. The performance recognition using the reconstructed images was 76.55%.


Power Spectral Density
log PSD
Frequency (Hz)
Frecuency band encoding
visual representation
Multimodal
representation

a)


Input
Brain data
encoded
White noise
Convolutional Layers
512x55x55
512x27x27
256x27x27
256x13x13
128x13x13
2x2
5x5
2x2
3x3
3x3
Pooling Layers
Encoder
Deconvolutional Layers
512x55x55
256x55x55
256x27x27
128x27x27
2x2
3x3
2x2
5x5
Unpooling Layers
Decoder
Output
Reconstructed
Brain data
encoding
Reconstructed
Image

b)

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Computational Brain and Neuroscience-Inspired Artificial Intelligence

Customisation of automated ML-based ICA-filtering

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Independent component analysis(ICA) is widely used for electrocorticography cleaning, but which ICA-components to be deleted is the question of expert choice and related to many factors (expirience, experiment design, etc). The huge amount of components to be marked made this marking work exhausting. We propose the ML-metod of automated marking, which can be teached by each expert to his own marking style.

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Computational Brain and Neuroscience-Inspired Artificial Intelligence

OPTIMIZATION OF DEEP BRAIN STIMULATION IN STN AMONG PATIENTS WITH PARKINSON'S DISEASE USING A NOVEL EEG - BASED TOOL

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Introduction

While the positive effects that deep brain stimulation (DBS) of the subthalamic nucleus (STN) exerts on motor functions in patients with Parkinson's disease (PD) are well known, not all patients respond similarly to the treatment. One plausible explanation is the numerous combinations between the chosen DBS electrode contacts and programming settings that include voltage, pulse width and frequency. Consequently, on average, finding the setting for optimal symptom control requires on average 6 sessions over 6 months.

The current study aims to develop an innovative method for objective differentiation between the locations of the four DBS contacts in the various parts of the STN as a first step towards automated treatment optimization, using a novel EEG-based tool called BNA (Brain Network Activation).

Methods

128-channel EEG was recorded from 17 DBS treated PD patients. Low-frequency stimulation at 2-5 Hz was applied to each of the four DBS contacts in the assorted parts of the STN (*Zona Incerta*,N=23, DLOR,N=23, VMNR,N=19) for several minutes. A total of 2000–2400 EEG epochs, aligned to stimulation onset, were averaged to produce a DBS Evoked Response per DBS contact. The DBS BNA was calculated for a predefined time-window of 50–100 ms after stimulation onset.

Results

The DBS-Evoked Response significantly differentiated between the *Zona Incerta* contact to the DLOR and VMNR contacts in the medial frontal central scalp area for the amplitude and latency measurements (F=13.1,(****) p<0.0001, 1-way repeated measures ANOVA); (F=9.4,(***) p<0.0003, 1-way repeated measures ANOVA)

Conclusions

We showed that by using scalp EEG we can distinguish between DBS contacts located in the STN area. This novel objective non-invasive measure will potentially transform the time-consuming DBS calibration into a quick and efficient optimization process.

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Digital Therapeutics

MACHINE LEARNING-BASED ELECTROPHYSIOLOGICAL MEASURES FOR MEMORY ASSESSMENT IN LATE LIFE

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The number of older adults with dementia is projected to rise world-wide, and our current capabilities for assessing cognitive changes as adults age are expensive and inadequate. Brain Network Activation (BNA) uses well-established electroencephalography (EEG) technology to generate information regarding brain function and health. To date, this technology has not been assessed in older adult populations. The current study aims to utilize BNA technology and machine learning techniques to reliably assess memory-related abilities in older adults and detect deterioration over time.
Research takes place in The Villages, an active-lifestyle community in Central Florida. Study participants underwent an in-person comprehensive health assessment and were stratified into 1 of 5 study arms [healthy, treated depression, multi-morbid, early Alzheimer's Disease (AD), and Mild Cognitive Impairment (MCI)]. Cognitive testing was conducted using the Registry for Alzheimer's Disease Assessment Battery's Word List Task and a delayed-match-to-sample memory task. Subjects underwent an auditory-oddball event-related potential (ERP) recording and BNA scores were generated. Canonical-correlation analysis (CCA) was employed to optimize the relationship between the BNA set of scores and performance on the cognitive tests. Once developed, the composite score was validated on a held-out dataset including normative cognition and memory impairment groups.
Findings show significant correlations between the composite BNA score and the composite memory performance score on both the training set and a held-out test set of subjects with normative cognition. Further, the model could clinically distinguish between subjects with normative cognition and MCI/early AD subjects.
Results show the potential of BNA as a tool for objective cognitive assessment and monitoring of cognitive changes over time. Further, this approach can potentially be expanded, allowing the creation of biomarkers for various other cognitive domains, such as attention and executive functioning.

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Digital Therapeutics

Fighting the Opioids Crisis in Migraine with Neuromodulation Digital Therapeutics

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INTRODUCTION

The Neurolief SP-301 Study, evaluated the clinical performance and safety of self-administered treatment for migraine using combined occipital and trigeminal neuromodulation (Neurolief Relivion™), in a prospective, randomized, double-blind, parallel-group, sham controlled clinical investigation.

Methods and Material

The Relivion™ is a head-mounted device designed to concurrently modulate major neural pathways in the head region for treatment of migraine (Fig.1).

It consists of a headset which integrates three pairs of output electrodes which come in contact with the subject scalp at the occiput (one pair) and the forehead (two pairs). The electrodes deliver the stimulation pulses produced by the electronic circuit to the subject's scalp. The frontal electrodes stimulate the Trigeminal (Supraorbital & Supratrochlear) nerve branches and the posterior electrodes stimulate the Greater Occipital nerve branches bilaterally (Fig. 2).

RESULTS

A total number of 55 eligible and consented subjects were randomized to the study.

Pain decreased significantly more in the treatment group compared to the sham group at all time points (group difference at 1-hour- **41.38%** 95%CI: [**20.57%**;62.18%], p-value: 0.0002, at 2-hours- **32.84%** 95%CI: [2.88%;62.80%], p-value: 0.0324, at 24-hours- **36.21**% 95%CI: [5.46%;66.96%], p-value: 0.0220).

Responders rate was also statistically significantly higher in the treatment group than in the sham group at 1-hour (**66.7%** ver. 20%, p-value 0.0014), 2-hours (**66.7%** ver. 32%, p-value 0.0227) and 24-hours (**78.3%** ver. 48%, p-value 0.0401). The difference between the two study groups in consumption of rescue medications and in pain free endpoints did not reach statistical significance, although **pain free** at 2-hours was more than twice as higher in the treatment group compared to the sham group (**41.7**% ver. 20%, respectively). (Fig. 3).

CONCLUSIONS

The results of this randomized, double blind, sham-controlled study demonstrate that self-administered, combined occipital and trigeminal neuromodulation by the Relivion™ device, is a safe and effective treatment of migraine.

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BrainT19-0039
Poster Presentations - March 4-5 - Exhibition Hours

Digital Therapeutics

MULTIMODAL BRAIN-COMPUTER INTERFACE BASED ON ARTIFICIAL INTELLIGENCE FOR REHABILITATION OF PEOPLE WITH MOTOR DISORDERS

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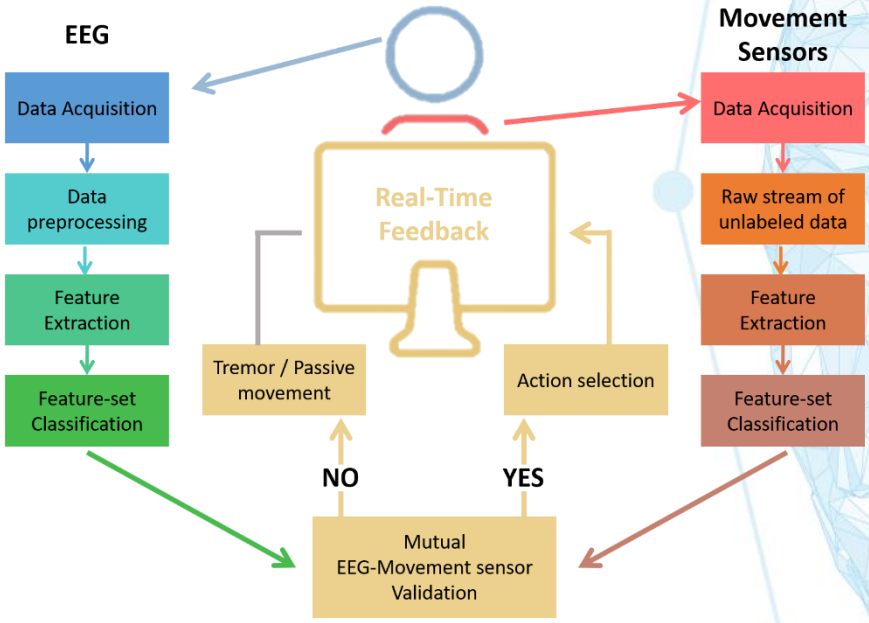
The project's objective is to develop a safe and reliable solution that would improve quality of life of people with severe movement. The solution is a multimodal brain-computer interface system for touchless control of devices and motor rehabilitation, which performs non-invasive decoding of brain and body signals using artificial intelligence methods. The project aims to solve the problem of improving efficiency of rehabilitation for patients with motor disorders (after stroke, spinal cord injury, and traumatic brain injury) using a non-invasive, portable and affordable system.

A multimodal real-time BCI prototype combining brain and body signal analysis has been developed. It is based on parallel acquisition and decoding of EEG and inertial measurement unit (IMU) signals, parallel feature extraction, classification and mutual validation of decoded motor commands. The system performs following main steps: 1) real time acquisition of EEG and IMU signals; 2) signal processing; 3) advanced feature extraction (including principal component analysis, spectrum analysis, wavelet transform and feature selection); 4) decoding of motor commands by means of classifiers based on machine learning; and 5) control of devices. A detailed block diagram of the developed system is shown in Figure.



Decoded motor commands in real time might be applied to control of assistive devices and specialized applications. The basic principle of the multimodal system is to use mutual validation of motor command decoding obtained from both IMU and EEG pattern recognition. If one classifier recognizes the pattern corresponding to a motor command, the other classifier has to validate it, with minimal time delays. Within the scope of the project special neurofeedback applications in game form were developed and paired with the prototype.

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Other

MIRROR NEURON SYSTEM AND MOTOR PERFORMANCE

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Cortex and cortical function can be regarded as modular, with separate areas involved in processing sensory information and the initiation of motor movement. The blood supply supporting cortex is, like the brain itself, modular. Disruption in blood flow leads to a multiplicity of dysfunctions like the frequent co-occurrence of aphasia and right upper limb hemiparesis.

Patients with Broca's aphasia show slower and poorer motor recovery of right arm compared to non-aphasic ones. Different causes were summoned to explain the difference in recovery.

Our theory, contrary to other conclusions, is that speech impairment is indicative of damage to Brodmann area BA45 but that the motor deficits are due to damage to the proximal, but functionally discrete area BA44. BA44 is a multisensory area. But experiments on tone-deaf or stutters, radiological tools like fMRI and DWI, studies of the neuro-ontogeny and development in babies, findings of genetic, epigenetic and embryology, all point to BA44 playing a central role in visuo-motor integration.

The presence of mirror neurons in BA44, enables the use of visual input to improve motor performance. Therefore, either watching professional top sport players or videos of them playing, will engage the mirror neurons system with the result of a better performance.

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Other

RISK FACTORS FOR VERTEBRAL ARTERY STENO-OCCLUSIVE DISEASE.

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BACKGROUND
Diabetes mellitus, hypertension and smoking have been described as risk factors for carotid artery disease and cerebrovascular disease in general. We performed a case control study to examine the effect of hypertension, smoking, and diabetes mellitus including other factors which may increase the risk of vertebral artery disease (VAD).
METHODS
Medical records of all aged 18 years or older who had angiographically confirmed VAD 50% were reviewed. Demographic and associated risk factors were ascertained. Controls were selected from the National Health and Nutrition Examination Surveys matched according to age, sex, and ethnicity. A step wise logistic regression was performed to identify the effects of risk factors on occurrence of VAD.
RESULTS
There were 56 patients with cerebral angiography confirmed VAD with mean age 66.0 ±SD 12.5 years; 55.4% were men. There were 747 exact controls matched from the NHANES database. Hypertension (odds ratio [OR], 5.0; 95% CI, 2.3 – 10.7), diabetes mellitus (OR, 3.3; 95% CI, 1.9 – 5.7), hyperlipidemia (OR, 4.6; 95% CI, 2.1 – 10.0), coronary artery disease (OR, 4.6; 95% CI, 2.6 - 8.4) and past cigarette smoking (OR, 3.3; 95% CI, 1.9-5.9) were associated with increased risk of VAD even after adjusted for age.
CONCLUSION
Hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease and past cigarette smoking increase the risk for development of VAD. The increased risk persists even after cessation of cigarette smoking, which suggests the importance of early abstinence from smoking and controlling all mentioned risk factors.

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Other

NEAR INFRARED ASSESSMENT OF BRAIN DISEASE

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Near Infrared Spectroscopy (NIRS) enables non invasive recording of the microvascular response to cortical activity. It uses light, delivered and collected from the brain using optical fibers, to measure the concentration of hemoglobin (oxygenated and deoxygenated) in specific cortical volumes. Functional NIRS (fNIRS) assess the time dependent concentration signals, similarly to the BOLD analysis of fMRI. Therefore, assessment of functional connectivity can be performed using the NIRS signals.
We have compared the resting-state functional connectivity maps, collected from six healthy subjects and six patients diagnosed with major depression (MDD). As the raw signals are contaminated by systemic contributions, we have used a new pre-filtering method, that have not been used in the analysis of fNIRS. This method, based on the Hilbert-Huang Transform (HHT), enables to discard the systemic contributions and focus on the brain related signals. Figure 1 shows the resulting connectivity maps for two subject – one healthy and one with MDD. The NIRS optodes number 1-12 are placed over the right parietal cortex, and optodes number 13-24 are placed over the left parietal cortex.

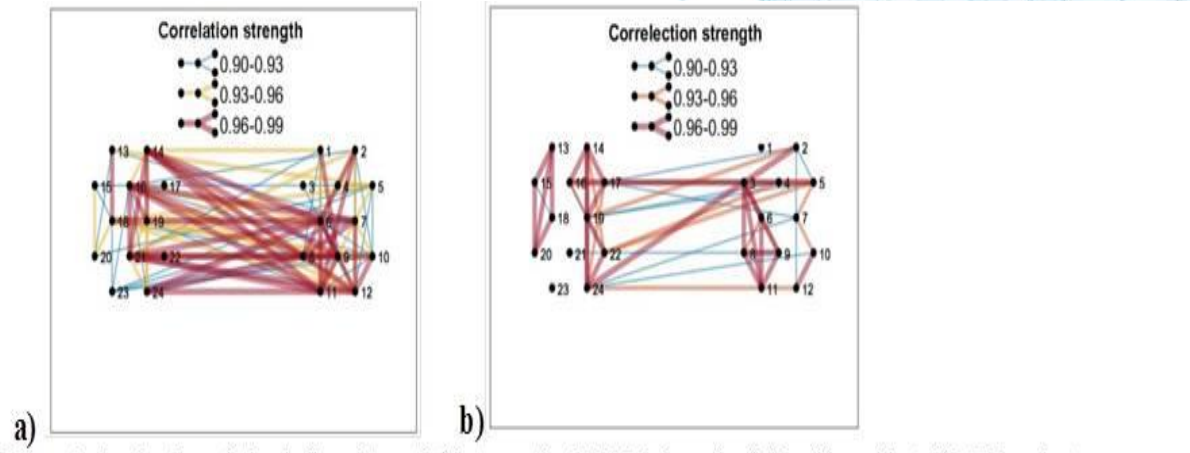

Figure 1: Graph of correlation indices (strengths) between the 24 NIRS channels of a) healthy subject, b) MDD patient

Looking at homologous connectivity maps, following HHT pre-filtering, there is a clear discrimination, for each individual subject, between healthy and diseased brains. Healthy subjects exhibit a high correlation index between most areas, whereas MDD patients exhibit a low connectivity.
Our preliminary results demonstrate that fNIRS resting-state connectivity, with appropriate pre-filtering, can be used to assess the health of individual brains. In the future this technology can be used to objectively assess major depression, or the progress of an individual patient receiving therapy. Thus it may be applied in parallel to brain stimulation therapy for MDD, and provide neuromarkers that objectively quantify the difference between a healthy and a diseased brain.

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BrainT19-0024
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Other

IMAGING AND TRACKING EXOSOMES WITHIN THE BRAIN USING GOLD NANOPARTICLES

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Exosomes are emerging as effective therapeutic tools for various pathologies. These extracellular vesicles can bypass biological barriers, and can serve as powerful drug and gene therapy transporters. However, the progress of therapy development is impeded by several challenges, including insufficient data on exosome trafficking and biodistribution and the difficulty to image deep brain structures *in-vivo*. Herein, we established a method for noninvasive *in-vivo* neuroimaging and tracking of exosomes, based on glucose-coated gold nanoparticle (GNP) labeling and computed tomography imaging. Labeling of exosomes with the GNPs was achieved directly as glucose-coated GNPs were uptaken into MSC-derived exosomes (MSC-exo) *via* an active, energy-dependent mechanism that is mediated by the glucose transporter GLUT-1 and involves endocytic proteins. Next, we determined optimal parameters of size and administration route; we demonstrated that 5 nm GNPs enabled improved exosome labeling and that intranasal, compared to intravenous, administration led to superior brain accumulation and thus enhanced *in-vivo* neuroimaging. Furthermore, we used this technique to track the migration and homing patterns of intranasally administrated MSC-exo in different brain pathologies, including stroke, autism, Parkinson's disease and Alzheimer's disease. We found that MSC-exo specifically targeted and accumulated in pathologically-relevant brains regions up to 96 hrs post administration. Our results indicate that the homing of MSC-exo in the brain is pathology-specific, and inflammatory-driven. Thus, this exosome labeling technique can serve as a powerful diagnostic tool for various brain disorders and could potentially enhance exosome-based therapy.

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Other

ISLET-BASED INSULIN DELIVERY TO THE BRAIN INDUCES LONG-TERM COGNITIVE IMPROVEMENT IN RATS WITH SPORADIC ALZHEIMER'S DISEASE

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Background. Alzheimer's disease (AD) is associated with brain insulin resistance. Insulin delivery to the brain can be a promising therapy for AD. However, efficient and safe technology for insulin delivery to the brain has not been developed yet. Recently, we showed that a small number of pancreatic islets implanted into the cranial subarachnoid space increased brain insulin content and improved cognitive functions of rats with sporadic AD (*J Alzheimers Dis. 2018;65(4):1445*). In the current study, we investigated the long-term effect of intracranial islet transplantation on cognitive functions in rats with AD.

Methods. Sporadic AD was induced in inbred Lewis rats by intracerebroventricular administration of streptozotocin (icv-STZ). 2 months after icv-STZ, 100 syngeneic islets were transplanted into the cranial subarachnoid space. 6 months after islet transplantation, cognitive functions were assessed by Morris water maze test and islet graft survival was evaluated by immunohistochemical and biochemical methods.

Results. 6 months after islet transplantation, spatial learning and memory in transplanted rats were significantly better than in the sham-operated icv-STZ rats. No significant differences in the locomotor activity between transplanted and non-transplanted icv-STZ rats were detected. Neither icv-STZ nor grafted islets altered peripheral glucose homeostasis. The grafted islets showed intact morphology, intensive staining of insulin and glucose transported 2 (Figure).

Conclusion. Intracranial islet transplantation provides an efficient and safe approach for insulin delivery to the brain, leading to a long-term attenuation of AD cognitive dysfunctions.

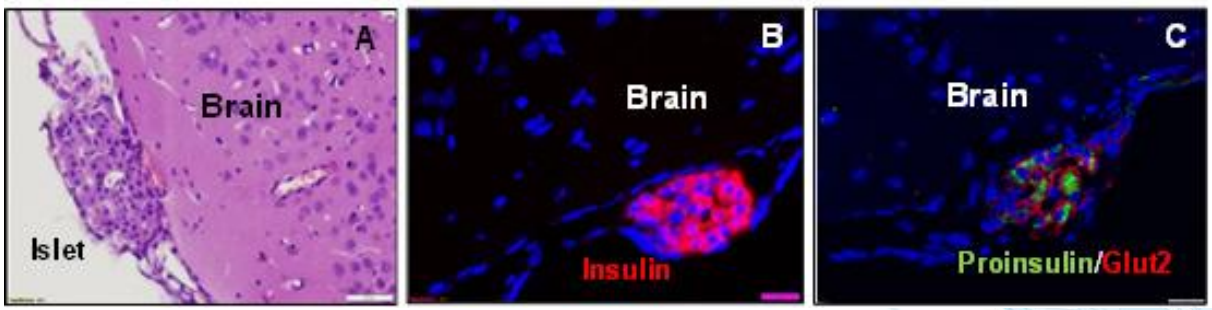

Figure. Morphology (A), insulin (B) and glucose transporter 2 (C) staining of islets grafted into cranial subarachnoid cavity of icv-STZ rats.

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Other

PROMOTING THE EVERY-DAY USE OF VISUAL-TO-AUDITORY SENSORY SUBSTITUTION DEVICES IN BLIND INDIVIDUALS – SUCCESSFUL USE IN THE PRESENCE OF ENVIRONMENTAL NOISE

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Visual-to-auditory Sensory Substitution Devices (SSDs) are a family of non-invasive devices for visual rehabilitation aiming at conveying whole-scene visual information through the intact auditory modality. Although proven effective in lab environments, the use of SSDs has yet to be systematically tested in real-life situations.

To start filling this gap, we here tested the ability of expert SSD blind users (N=9) to filter out irrelevant background noise while focusing on the relevant audio information, namely a task often described as a major bottleneck regarding the adoption of SSDs in real-life. Participants performed a series of geometric shapes' identification tasks via the EyeMusic visual-to-auditory SSD (i.e., shape, color, and conjunction of the two features). Performance was compared in two separate conditions: silent baseline versus irrelevant background sounds from real-life situations, using the same stimuli in a pseudo-random balanced design. Although participants described the background noise as disturbing, no significant performance differences emerged between the two conditions (i.e., noisy; silent) for any of the tasks. In the conjunction task (shape and color) we found a non-significant trend for a disturbing effect of the background noise on performance. These findings suggest that visual-to-auditory SSDs can indeed be successfully used in noisy environments and that users can still focus on relevant auditory information while inhibiting irrelevant sounds.

In addition, we have preliminary results on the success of different SSD training materials and training strategies we developed, ultimately further promoting the suitability of SSDs for everyday use. Specifically, we showed that blind expert EyeMusic users can learn to recognize many real-life objects. We have also shown that the basics of the EyeMusic can be successfully learned via a self-training platform (http://brain.huji.ac.il/launch/Home/create_user_short). All of these attempts take a step towards the actual use of SSDs in real-life situations while potentially impacting rehabilitation of sensory deprived individuals.

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Other

EEG-based Prediction of Cognitive Load in Intelligence Tests

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Measuring and assessing the cognitive load associated with different tasks is crucial for many applications, from the design of instructional materials to monitoring the mental well-being of aircraft pilots. The goal of this paper is to utilize EEG to infer the cognitive workload of subjects during intelligence tests. We chose the well established advanced progressive matrices test, an ideal work-frame because it presents problems at increasing levels of difficulty, and has been rigorously validated in past experiments. We train classic machine learning models using basic EEG measures as well as measures of network connectivity and signal complexity. Our findings demonstrate that cognitive load can be well predicted using these features, even for a low number of channels. We show that by creating an individually tuned neural network for each subject, we can improve prediction compared to a general model and that such models are robust to decreasing the number of available channels as well.

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Other

Dissociation between Reaction Time and Pupil Dilation in the Stroop Task

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It has been suggested that the Stroop task gives rise to two conflicts: the information conflict (color vs.word meaning) and the task conflict (name the color vs. read the word). However, behavioral indications for task conflict (RT congruent condition longer than RT neutral condition) appear under very restricted conditions. We conducted Stroop experiments and measured RT and pupil dilation. The results show a clear dissociation between RT and pupil dilation. We found the regular RT pattern—large interference and small, non-significant facilitation. In contrast, pupil dilation showed information conflict—larger pupil dilation to incongruent than to congruent and neutral conditions—and task conflict—larger pupil dilation to the congruent than to the neutral condition. Moreover, pupil indications for task conflict appeared earlier than indications for the information conflict. These results suggest that pupil changes could indicate conflict even in the absence of behavioral indications for the conflict.

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Other

Addictive eating in morbid obesity: behavioral and electrophysiological characteristics

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Background: Obesity is a growing public health problem with staggering economic and social implications. Theories explaining the propensity to overeat have been primarily based on behavioral studies and did not yield effective interventions which can produce long-term weight loss. The incentive sensitization theory to obesity suggests that a neurocognitive malady is at the center of this condition, where obese individuals are over-sensitized to external food cues, thereby occasionally express food addiction (FA). FA can be measured with the Yale Food Addiction Scale (YFAS) and may indicate a distinguished obesity phenotype. **Methods:** 31 obese adults (19 FA obese [FAOB]), completed several behavioral and electrophysiological measures, including the YFAS, a Food Stroop task and a measure of alpha power during a 5-min electroencephalographic (EEG) recordings at rest. **Results:** Compared to non-FA obese (NFAOB), FAOB showed left Prefrontal cortex (PFC) asymmetry, evident by lower left compared to right PFC alpha power at rest (t= -38.54,p=.001). FAOB also showed a greater P200 component to images of high caloric food (HCF) compared with non-food (NF) items (t=-158.58,p=.04) during Food Stroop task. Similarly, FAOB showed greater reaction time to the Stroop stimuli, following the presentation of HCF vs. NF images (t =4.32,p =.05).
Discussion: Obesity with FA found to be associated with a specific and unique behavioral and electrophysiological markers. These markers implies pathological brain activity expressed by lower left PFC alpha power at rest and greater attentional bias which indicates the level of emotional reactivity to high-calorie food. Despite no differences in BMI, these findings point to a tendency towards food cue reactivity and impaired inhibitory control over eating in FAOB. The neurobehavioral distinction between FAOB vs. NFAOB found herein is novel and may help characterize FA, potentially leading to new treatment approaches to this obesity phenotype.

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Other

IN-VITRO INDUCED PLURIPOTENT STEM-CELL BASED NEURO-VASCULAR UNIT FOR DRUG SCREENING

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The Blood-Brain Barrier (BBB) constitutes a neuro-vascular unit (NVU), comprised of astrocytes, pericytes, neurons and brain microvascular endothelial cells (BMECs) – all of them interacting to form a barrier between the circulatory system and the Central-Nervous System (CNS). One of the main challenges in drug development today is on one hand, enhancing CNS-targeted drug delivery to the CNS, and on the other, preventing unwanted substances from reaching there. Marked differences in BBB physiology and transport mechanisms across species limit the relevance of animal models for predicting CNS penetrability.

Induced pluripotent stem-cells (iPSCs) provide an attractive source of BMECs. Here, we are developing an in vitro dual-compartment NVU system based on Transwell® and microelectrode array (MEA) systems. The top, endothelial compartment is seeded with iPSC-derived BMECs that form a continuous monolayer, expressing tight-junction proteins over a porous membrane, which achieve physiologically relevant transepithelial electrical resistance (TEER). The bottom, neural compartment contains primary brain cells isolated from rat striatum, seeded on a Microelectrode Array (MEA), allowing real time electrophysiological measurements. Our preliminary results show that iBMECs growing over primary striatal rat cells displayed increased TEER compared with iBMECs growing over fibroblasts or as a monoculture. These results demonstrate the potential of our approach to simulate physiological conditions, and together with the ability of using multi-well plates containing multiple systems to develop a high throughput platform for drug screening and development.

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Other

Early Detection of Wake-up Stroke using Wearable Sensors: Preliminary Study

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[Background]

Stroke is the fifth cause of death and the leading cause of physical disability in the United States. For effective acute management, early detection of stroke is essential. But, detection of wake-up stoke is difficult, and there is no sensing system to help. Hemiplegia/paresis is the most frequent clinical presentation of stroke. It is natural to anticipate decreased motion in the hemiparetic side.

In this present study, we investigate whether degree of asymmetry of motion positively correlates with the severity of hemiparesis.

[Method]

Subjects are four patients with hemiparesis due to cerebral infarction. We used a wearable system consisting of two finger-bands and two wristbands to detect the motion of each body part. Each band consists of 3-axis accelerometer sensors, and our system records motion while the patients sleep at night. For sleep data analysis, we first calculated the number of motions above a heuristic threshold on a 60-minutes sliding window in each side. Thereafter, we generated an absolute value of a ratio between the affected side sliding window and none-affected side sliding window, i.e., asymmetric ratio. Descriptive statistics were used according to muscle strength.

[Result]

Table 1 shows an asymmetric ratio value in finger-bands and wristbands according to MMT.

Table 1 Asymmetric ratio in sleep data of four hemiparesis patients

Patient Number	MMT (Right/Left)	Asymmetric ratio on Finger-bands (mean±SD)	Asymmetric ratio on Wristbands (mean±SD)
1	5/2	3.94±1.48	4.49±1.81
2	4/5	3.43±1.73	1.99±2.36
3	5/4	1.49±0.61	1.78±1.28
4	5/5	1.28±1.10	1.31±1.04

MMT: manual muscle test of elbow flexor

[Conclusion]

Asymmetric ratios were increased according to the severity of hemiparesis. Asymmetric ratio using motion sensor may be helpful to detect wake-up stroke.

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Other

CAN OPTICAL MAGNETOENCEPHALOGRAPHY REPLACE INTRACRANIAL RECORDINGS? THE CASE OF MOVEMENT-RELATED RESPONSES.

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Recently introduced Optically Pumped Magnetometers (OPMs) are a new kind of sensors for magnetoencephalography (MEG) that do not require cryogenic cooling and can be placed directly on the scalp. OPMs are expected to improve the SNR and spatial resolution of MEG and open new avenues for MEG research such as recording in freely moving subjects. However, whether they can record signals qualitatively different from those afforded by the existing MEG is an open question.

One type of signal which is known to exist in the brain and is of special interest for research and clinical applications is wideband spectral responses associated with cortical activation seen in electrocorticography (ECoG) in the high gamma band (above 50Hz). These responses are used clinically for mapping of 'eloquent cortex' – areas active during movement and speech. Movement-related high gamma responses are also seen in MEG, but there they are band-limited and do not extend above ~100Hz. It is not clear whether this is because MEG SNR is too low at high frequencies or because the phenomenon seen in MEG is truly band-limited and distinct from that of ECoG.

To determine whether the movement-related responses in OPM MEG are more similar to ECoG or to conventional MEG we used OPMs to record MEG from sensorimotor areas during clenching and releasing of the contralateral fist. We compared the movement-related spectral changes to those recorded from the same subject with conventional MEG and to publicly available human ECoG dataset with the same task.

We found that OPM MEG can record movement-related oscillatory responses similar to conventional MEG and the spectral profile of the responses is similar between two MEG variants and different from ECoG.

Our results support the suggestion that wideband gamma responses predominantly seen in ECoG and narrow-band responses seen in MEG correspond to distinct physiological phenomena.

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Other

Early Blood-Brain Barrier Dysfunction Predicts Neurological Outcome Following Aneurysmal Subarachnoid Hemorrhage

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Background

Disease progression and delayed neurological complications are common after aneurysmal subarachnoid hemorrhage (aSAH). We explored the potential of quantitative blood-brain barrier (BBB) imaging to predict disease progression and neurological outcome.

Methods

Data were collected as part of the Co-Operative Studies of Brain Injury Depolarizations (COSBID). We analyzed retrospectively, blinded and semi-automatically magnetic resonance images from 124 aSAH patients scanned at 4 time points (24-48 h, 6-8 days, 12-15 days and 6-12 months) after the initial hemorrhage. Volume of brain with apparent pathology and/or BBB dysfunction (BBBD), subarachnoid space and lateral ventricles were measured. Neurological status on admission was assessed using the World Federation of Neurosurgical Societies and Rosen-Macdonald scores. Clinical outcome at 6 months or later was assessed using the extended Glasgow outcome scale.

Findings

Based on repeated volumetric measures of pathological brain tissue and CSF, patients were categorized as having either progressive (increased pathology; 64%) or non-progressive (36%) disease course. No differences were found between the two groups in aneurysm locations, neurological status on admission, initial brain pathology or treatment (coiling or clipping). Females were older and more likely to have a non-progressive course compared to males ($p<0{\cdot}01$). Progressive course was associated with worse outcome at ≥6 months. A substantial brain volume with BBBD was found already 24-48 h after admission, and persisted at all time points. Brain volume with BBBD was significantly larger in patients with progressive course. BBBD increased the likelihood of a normal brain tissue to become pathological ($p<0{\cdot}001$). A multiple-linear regression model revealed a significant power for BBBD in combination with RMS at 24-48 h in predicting outcome (receiver operating characteristic area under the curve, 0·804; $p<0{\cdot}001$).

Interpretation

We suggest that early identification of BBBD may serve as a key predictive biomarker for neurological outcome in aSAH.

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Other

Prevention and Intervention of Stroke Risk with an Artificial Intelligent System

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Background

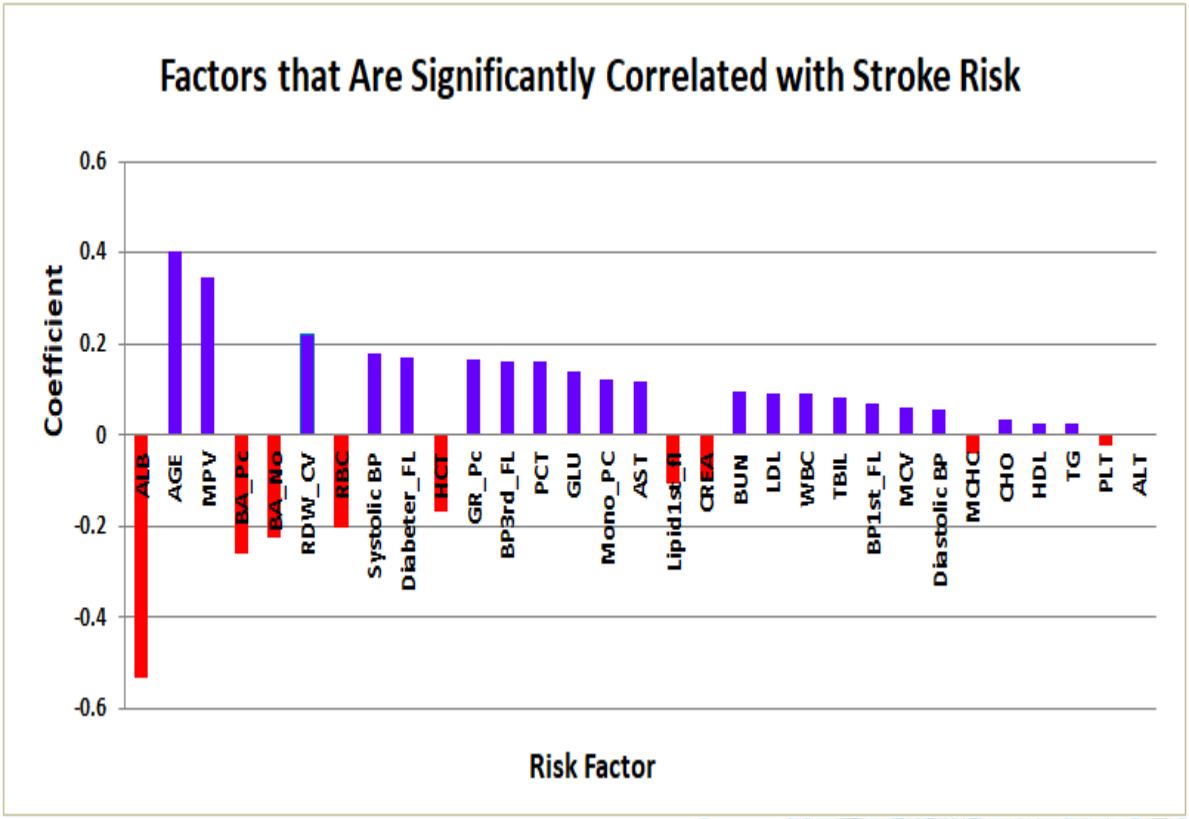
Worldwide prevalence of stroke was 25.7 million, with 10.3 million people having a first stroke. According to American Stroke Association, 80% of strokes can be prevented, therefore, prevent and intervene stroke from happening would save millions of lives worldwide. The purpose of this research is to provide a simple, convenient and economical method to help people prevent and intervene stroke.

Method

A total of 612,952 subjects including 21,091 stroke patients and 591,861 normal people were involved in the study. The data were used in the study including demographics, CBC, CMP and Lipids data. Analysis of covariance, logistic analysis, discriminant analysis, deep learning and simulation were used to identify the significant factors and to build the stroke risk prediction model and the significant level was set at $p < 0.05$. Machine Learning, Neural Network, SAS and SPSS were used as the data mining and statistical analysis tools. The strategies of “The Art of War” were used to develop personalized Stroke prevention strategies to help people know their Stroke risk, know high risk factors and preciously intervene and intercept Stroke risk.

Results

The research showed that blood test results of CBC, CMP and Lipids are significantly correlated with the stroke risk and treating the abnormal results would lower stroke risk (see Table below for details). Among 31 parameters, Albumin (ALB), age, mean platelet volume (MPV), percentage of basophils and red cell distribution width are top predictors that can predict and identify high stroke risk people (see Table below for details). The predicting accuracy was 98.1% and the clinical verification rate was 95.9%.



Conclusion

The research provides a simple, effective way to help people stop stroke risk by treating abnormal blood test results of CBC, CMP and Lipids and changing lifestyle.

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BrainT19-0031
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Other

THE EFFECTS OF DUAL TASKING AND AGING ON EVENT RELATED POTENTIAL (ERP) COMPONENTS OF GAIT CYCLE

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Background: Walking in everyday life requires coping with challenging conditions such as dual-tasking, and is thus considered to be controlled by higher cognitive processes. Electroencephalogram (EEG) can be useful in investigating brain activity during real, dual-task walking. Our aim was to evaluate the effects of dual tasking on the event related potential components of the gait cycle.

Methods: 10 young adults (age: 33±6.5yrs; 50% women) and 10 older adults (age: 67.1±5.52yrs; 60% women) walked on a treadmill with audio oddball (dual-task) and without (usual walk), while wearing a wireless EEG cap and accelerometers on the ankles. Each heel strike extracted from the accelerometers was used as the event from which electrical brain activity pattern was calculated. Amplitude and latency of the ERP components from channel Pz were compared between and within groups using linear mix model analysis.

Results: The ERP components of gait cycle included four positive deflections. Older adults showed higher amplitudes than young adults, during usual and dual-task walking (p=0.012). Both groups showed higher amplitudes during dual-task as compared to usual walk (p=0.018). The latency of these ERP components were longer in older adults than young adults in both walking tasks (p=0.001). The mean amplitude was correlated with gait speed only in young adults (r=0.700, p=0.024), while among older adults, mean amplitude was correlated with MOCA scores (p=0.715, r=0.020).

Conclusions: These findings provide direct evidence on the effects of aging and task complexity on electrical brain activity during walking. The ERP amplitude mirrors the amount of neurons activated and synchronized during the processing of incoming information. Therefore, the higher amplitudes seen during dual tasking likely reflects the extended well synchronized resources required for walking in challenging conditions. This effect was even larger in older adults indicating an ageing effect potentially reflecting a deterioration of brain capacity in ageing.

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Other

IMT, FMT, homocysteine and serum hepcidin in obstructive sleep apnea

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Obstructive sleep apnea syndrome (OSA) is defined as a combination of symptoms as a result of intermittent, recurrent constraint and / or complete airway overhead airway overflow (sleep disturbance). OSA is associated with the development of insulin resistance, arterial hypertension, metabolic syndrome, systemic atherosclerosis and increased cardiovascular risk. 49 patients with OSA were included; age 44.1 ± 7.7. Their results were compared to sex and age matched healthy control. CBC, serum iron, ferritin, hsCRP, hepcidin, homocysteine and vitamin B12 were measured in the included groups. IMT and FMT were used for atherosclerotic changes evaluation. We found increased serum hepcidin levels in OSA patients with IMT and FMD changes (129.9 ± 20.4 μg/L) compared to control group (20.9 ± 1.7 μg/L); $P<0.001$. A positive correlation was found in OSA patients with atherosclerotic changes between IMT and FMD to serum hepcidin levels ($r=0.811$, $r=0.829$, resp.; $P<0.005$). Serum hepcidin correlates positively to homocysteine and vitamin B12 in OSA patients ($r=0.809$, $r=0.855$, resp.; $P<0.01$). Brain-vascular disease risk factors are connected to obstructive sleep apnea syndrome. Disregulation of iron homeostasis is one of the main risk atherogenesis factors. Early hepcidin quantification might predict an atherosclerosis occurrence in OSA patients, which might be very important for better clinical diagnosis and practice.

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