CNB Newsletter
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CLINICAL NEUROSCIENCE BERN

Dear CNB members,

With the CNB Newsletter, we intend to inform you about upcoming CNB events, ongoing projects and give insights into the research topics of selected CNB members.

We hope you enjoy reading the November 2020 edition.

Prof. Dr. Tobias Nef
President CNB

① 15th CNB Annual Meeting 2020 Review

Friday, 23th of October 2020

The 15th annual meeting of the Clinical Neurosciences Bern was held with the overall topic "brain repair" and it was the first online annual meeting.

This year's program included two Key-notes, the CNB group leader's meeting and an online poster session.

Professor Sebastian Jessberger from the Brain Research Institute of the University of Zurich talked about the Molecular and functional diversity of adult neural stem cells.

The second Key-note from Professor Roland Wiest from the Institute of Diagnostic and Interventional Neuroradiology at the Inselspital Bern thematized the imaging perspective of brain injury and repair.

The online poster session in the afternoon provided young researchers with the opportunity to present their ideas and research achievements by talks.

The winners of the poster price awards are:

Patricia Renz et al. (Category: Basic research animal)
Title: "Deciphering astrocyte polarization in perinatal white matter injury and its role in disease pathogenesis"

Romain Ghibellini et al. (Category: Basic research human)
Title: "Hypnagogic states are quite common: Evidence from a Swiss population"

Brigitte Kaufmann et al. (Category: Clinical Research)
Title: "Eye know about your neglect: Eyetracking during free visual exploration (FVE) is sensitive and reliable to detect neglect"

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② Selected Research Groups

PD Dr. phil. Andreas Altorfer

Music and Emotion
University Hospital of Psychiatry

Through the topic of the research group it is evident that this domain has to be treated in an interdisciplinary way. Music and emotion are quite different concepts with the special impact that music can lead to emotions. Although emotions are heavily needed to play music, the inverse is not the topic of the research group. As head of this group I am musician, musicologist and psychologist and I try to combine these aeras of expertise to introduce - especially in music - a scientific approach that expands subjective rating with concepts of music theory and harmonic analysis. On the side of emotion special importance is attached to the physiological basis of emotions. Emotion attribution is not the main concern; however, emotions are named and can be identified using predictions that follow musical style, harmony, and interpretation in a performance.

Our research interests are to enlighten the relation between listening of music of different styles and the experience of emotional involvement. Music is a complex phenomenon that can be described in different ways using objective facts of progression in harmony, tonality, pitch, theoretical implications of music especially in tempo and variations in tempo (tempo rubato). Tempo variations usually named agogic playing consist in a kind of accent dealing with a lengthening of the time-value of notes or accenting a musical note or phrase by extending it slightly beyond its normal time value. Such playing may violate normal expectations in the progression of music pointing to important harmonic instances in contrast to a metronomic progression of music, played e.g. by a synthesizer. Expectancy violations usually are locations where emotional reactions are expected. Along with different interpretations of musical scores by soloists there is a wide range of possible ways to point to intrinsic factors in music that have different effects on emotions. Imagine how many different interpretations of Beethoven's piano Sonatas exist, with the option that any new one you hear may touch you in a new specific emotional way or leave you emotionally uninvolved.

Other locations of musical importance are harmonic modulations, characteristics of a used tonality, and musical time in the beat (3/4, 4/4, 9/8, etc.). Many of these special facts in music are described in theoretical literature about music in different centuries. Baroque style music has other rules and ideas about pitch and tonality than romantic style music, all has to be reflected in interpretations. In fact, there are many features of music that may determine the musical reception especially in terms of an affective involvement leading to emotional feeling, modulating the state of a psychological condition.

As an indicator for emotional processes physiological conditions of the body are important signs of a process that brings up in fact the prerequisites of an attribution of specific emotions like fear, joyfulness, sadness, easiness, contemplation or deep involvement. Physiological measurements we use as markers of emotional involvement are EKG in terms of investigations of Heart Rate (HR) and Heart Rate Variability (HRV) to trace HR changes, Pulse Volume (PV) to trace vessel changes in peripheral body parts, Skin Conductance Responses (SCR) to differ arousal and attention, respiration for an analysis of synchronicity between musical beat and retention of breathing, and EEG measurement to get insight in brain functions associated with musical progression of high resolution.

By investigating perceived and physiological arousal, interactions could be found between different parameters, such as sound intensity, subjective arousal rating, HR, formal elements (exposition, development, and reprise), and rhythmic variations. Compared with relaxation, music induces and modulates physiological arousal; this tendency reflects a basic concept of experienced emotions. Reported results in different studies indicate a remarkable interaction between sound intensity and subjective arousal. However, they are not the only parameters that influence the physiological modulation induced by pieces of music. Aspects of interpretation which in romantic music are mainly reflected in changes of rhythm and dynamic progression also influence physiological reactions (Mikutta et, al. 2013).

To show an overall effect of music listening to brain functions, physiological correlates are investigated to analyze continuous changes in subjective emotional states while listening to a complete music piece (the whole first movement of Beethoven's 5th symphony). Results indicate that a long piece of music is capable of inducing consistent changes in brain functional states associated with arousal and emotions. These state-changes were identified across individuals and therefore represent processes that can be observed independent from eventual individual differences in music preferences. Frontal asymmetry in the lower alpha-band, which may be associated with activations of subcortical limbic structures during periods of high arousal in music are found. The results indicate that music is a powerful emotional stimulus (Mikutta et al. 2012).

By including personality factors e.g. the status of sensation seeking, it could be shown that physiological evaluation of variations in time in different interpretations of Beethoven's "For Elise" modulates physiological reactions. Interpretations with high impact on underlying agogic clarification of harmonic progression show different reactions of subjects with high sensation seeking and low sensation seeking values. High sensation seeking subjects display a physiological readiness without specific modifications of HR along with accelerations or decelerations of beats, whereas low sensation seeking subjects show fine HR changes triggered by succeeding beats and deviations from regular beat. In this respect, low sensation seeking subjects only, may be sensible to rhythmic violations of expectancy as postulated by Krumhansl (2000; Krumhansl and Agres, 2008) and are therefore emotionalized. This result is supported by HRV data too (Mikutta et al. 2020).

Such different reaction of subjects with special traits and capabilities may be found in a comparison of physiological reactions between professional and amateur musicians. In EEG data it can be observed a mid-frontal theta frequency in professional musicians over the entire musical piece (first movement of Beethoven's 5th symphony) pointing to more intense emotional activity when listening to music. Different patterns of alpha (right frontal in the amateurs versus bi-occipital in the professionals), beta (central in the professionals), and delta activity (central in the professionals) are found during high arousal. In this respect, musical experience modulates brain function strengthening processes of emotional experiences during music listening (Mikutta et al., 2014).

Recent work is done to enlighten tonality factors in baroque and romantic music what is seen in music theory especially in 18th century as important marker of the emotional quality of music (Berkh, 1977; Marpurg, 1776). Additionally, physiological correlates of emotional involvement in music are investigated to find evidence how emotional experiences can be modified with listening to defined musical interpretations and genre. Such work can be seen as basis for therapeutic intervention using music in listening to physiological relevant interpretations that can modulate emotions.

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Selected publications:

- Beckh H. (1977). Die Sprache der Tonart in der Musik von Bach bis Bruckner. 3. Auflage, unveränderter, photomechanischer Nachdruck der 1. Auflage 1937, Urachhaus, Stuttgart.
- Krumhansl C.L, Agres K.R. (2008). Musical expectancy: The influence of musical structure on emotional response. Behavioral and Brain Sciences 31(5):584-585.
- Marpurg F.W. (1776). Versuch über die musikalische Temperatur. Johann Friedrich Korn, Breslau.
- Mikutta C.A., Altorfer A., Strik W., Koenig T. (2012). Emotions, arousal, and frontal alpha rhythm asymmetry during Beethoven's 5th symphony. Brain Topogr 25:423–430.
- Mikutta C.A., Schwab S.G., Niederhauser S., Würmle O., Strik W.K., Altorfer A. (2013). Music, perceived arousal, and intensity: psychophysiological reactions to Chopin's "Tristesse". Psychophysiology 50:909–919.
- Mikutta C.A., Maissen G., Altorfer A., Strik W.K., Koenig T. (2014). Professional Musicians Listen Differently to Music. Neuroscience, 268, 102-111.
- Mikutta C.A., Tereh A.D., Simon G. Schwab S.G., Strik W.K. & Altorfer A. (manuscript 2020, submitted) Cardiovascular Activity during Perception of Musical Rhythm: A Comparison of High and Low Sensation Seekers. Psychotherapy and Psychosomatics. 2017;86(1):60-61.
- Blaettler LT, Stewart JA, Gubler DA, Egloff N, von Känel R, grosse Holtforth M. Alexithymia moderates effects of psychotherapeutic treatment expectations on depression outcome in interdisciplinary chronic pain treatment. Journal of psychosomatic research. 2019;122:69-72.
- Gómez Penedo JM, Rubel JA, Blaettler LT, Schmidt SJ, Stewart JA, Egloff N, grosse Holtforth M. The Complex Interplay of Pain, Depression, and Anxiety Symptoms in Patients with Chronic Pain: A Network Approach. (submitted).

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Prof. Dr. Mauricio Reyes

Biomedical Neuroimage Analysis
University Hospital Bern

The research activities of the biomedical neuroimage analysis group focus on an interdisciplinary approach to research and develop advanced medical image analysis technologies, and related translational biomedical engineering technologies, to quantify, diagnose, and follow-up disorders related to the central nervous system.
In particular, areas of research include automated brain tumor image analysis technologies, stroke image analysis for new therapeutic stroke recovery technologies, radiomics research in neuroimaging to produce insights into the robustness of A.I technologies, and interpretability of deep learning technologies to enhance the trustability, adoption and safety of A.I technologies used in neuroimaging.

Since several years the group has focused on developing technologies to automate the task of brain tumor image analysis. Among these analysis tasks, lesion contouring is a time consuming and error-prone clinical task. Based on A.I technologies our group has developed methods and produced related translational technologies to automate the delineation of brain tumors. We have made these technologies available for the research community but also further developed them for future clinical use. In this regard, a unique feature of our translational developments has been in incorporating the capability of the technology to progressively adapt to changes in imaging modalities. In addition, the developed technologies feature an inclusive model, where state-of-the-art approaches worldwide can be fused to enhance performance and robustness. Beyond lesion contouring our current research activities lie on rethinking and challenging current A.I technologies such that they are optimized to the clinical end-goal. In these regards, in radiation oncology, we are investigating A.I learnability approaches targeted directly towards metrics derived from the clinical-end goals.

Radiomics is an emerging research area where image analysis methods are employed to mine imaging information to answer clinical questions. Our research in radiomics is focused in investigating patters of robustness of radiomics-based imaging biomarkers in multi-center studies where imaging variability is inherent. We have highlighted current challenges to setup robust radiomics analysis in brain tumor imaging, and proposed methodologies to compensate these issues when models trained in single-center datasets are employed for multi-center radiomics analysis.
Towards a better understanding and clinical adoption of medical imaging A.I technologies, our group is researching on interpretability approaches to leverage our understanding on the underlying learning mechanisms of AI systems, as well as to identify areas where their robustness is affected in clinical imaging scenarios. On a similar line of thought, our group has also investigated on the reliability of uncertainty estimates of AI-based automated delineation systems, where we have reported the current challenges and potential avenues towards safe and reliable utilization of these technologies.

Our research is based on a multidisciplinary approach where clinical experts, AI specialists and biomedical engineers thrive together towards improved medical imaging computing technologies.

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Recent Publications:

- Suter Y., Knecht U., Alao M., Valenzuela W., Hewer E., Schucht P., Wiest R., and Reyes M. Radiomics for glioblastoma survival analysis in pre-operative MRI: Exploring feature robustness, class boundaries, and machine learning techniques. Cancer Imaging, June 2020.

- Pinto A., Pereira S., Wiest R., Alves V., Reyes M., and Silva C. Combining unsupervised and supervised learning for predicting the final stroke lesion. Medical Image Analysis, In Press, 2020.

- Ermis E., Jungo A., Poel R., Blatti-Moreno M., Meier R., Knecht U., Aebersold D., Fix M., Manser P., Reyes M., and Herrmann E. Fully automated brain resection cavity delineation for radiation target volume definition in glioblastoma patients using deep learning. Radiation oncology, 15:1-10, 2020.

- Balsiger F., Jungo A., Scheidegger O., Carlier P., Reyes M., and Marty B. Spatially regularized parametric map reconstruction for fast Magnetic Resonance Fingerprinting. Medical Image Analysis, 64:101741, August 2020.

- Jungo A., Balsiger F., and Reyes M. Analyzing the quality and challenges of uncertainty estimations for brain tumor segmentation. Frontiers in Neuroscience, 14:282, 2020.

- Silva W., Cardoso J., and Reyes M. Interpretability-guided content-based medical image retrieval. In Medical Image Computing and Computer-Assisted Intervention - MICCAI 2020, October 2020.

- Reyes M., Meier R., Pereira S., Silva C., Dahlweid FM., von Teng-Kobligk H., Summers R., and Wiest R. On the interpretability of Artificial Intelligence in Radiology: Challenges and opportunities. Radiology: Artificial Intelligence, 2(3): e190043, 2020.

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③ Upcoming events

15. – 18. March 2021	Brainweek Bern 2021 *Gender & Brain*

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