Improving hearing and functioning in children and adults (Case study #1)

Deniz Başkent

NAME(S): Prof. D. Başkent
INSTITUTE AND PROGRAM: BCN, PCN
THEME: Auditory perception and cognition
PROJECT TITLE: Guided Audiomotor Exploration (GAME) music training for cochlear implant users (CIMU-GAME)

1. Why is this topic important? What is the challenge?

Hearing is important for the awareness of one's surroundings, but also for speech communication. The disruption of hearing perception can be devastating for the individual experiencing it. In children, hearing impairment can lead to developmental problems and delays in the acquisition of speech and language skills as well as social and emotional skills. In older adults, hearing impairment can lead to increased isolation, and possibly also to an increased risk of dementia. In Europe alone, there are some 34,4 million individuals reported to have hearing loss, with two out of three untreated[1]. WHO reported 466 million individuals with hearing loss worldwide, 34 million of whom are children[2].

Hearing devices, such as hearing aids and cochlear implants (CI), as well as other forms of hearing rehabilitation, help resolve some of the challenges related to hearing problems. However, these devices and programs are still not capable of entirely restoring normal hearing. Neurophysiological mechanisms of hearing loss are still not fully understood, and cochlear implants (CIs), where hearing perception achieved by means of electrical stimulation of the auditory nerve, are is still unable to entirely replicate normal hearing patterns .

1 https://www.hear-it.org/hearing-loss-in-europe
2 https://www.who.int/news-room/fact-sheets/detail/deafness-and-hearing-loss

2. What is needed to address this challenge? And how are you specifically addressing it? What is the approach you are going to take?

To provide truly affective help for hearing-impaired individuals of all age groups, an approach from various angles, including technical and clinical approaches, is needed. Manufacturers of hearing devices have been actively collaborating with health professionals to further improve hearing devices and produce a more optimal hearing experience for the user of the device. The current basic rehabilitation for hearing loss is based on training with speech materials, due to the importance of speech communication. However, within the Brain & Cognition Institute at the University Medical Center in Groningen, Prof. Deniz Başkent and her team are investigating a different approach: they are using music training for the rehabilitation of hearing loss. Based on previous research, they know that music training not only leads to enhanced music skills, but that it can also improve other aspects of auditory perception, such as the perception of vocal emotions and even speech understanding[3,4,5].

Since this approach demands a truly multidisciplinary perspective, their collaborative team consists of specialists from engineering, otorhinolaryngology, cognitive neuroscience, audiology, music neurocognition, and music pedagogy. The team is implementing GAME, an improvisation-based piano instruction method developed by Robert Harris from the Research Group Lifelong Learning in Music,

Prince Claus Conservatoire, for use with cochlear implant users. Our team will be investigating the potential benefits of GAME for their perception of speech and music, as well for their quality of life.

[3] Fuller, CD, Galvin III, JJ, Free, RH, Maat, B, Başkent, D, 2014. The musician effect: Does it persist under degraded pitch conditions of cochlear implant simulations? Front. Neurosci. 8:179.
[4] Başkent, D, and Gaudrain, E, 2016. Musician advantage for speech-on-speech perception. JASA-EL 139, EL51-EL56.
[5] Kaplan, EC, Wagner, AE, Toffanin, P, Başkent, D, 2021. Do musicians and non-musicians differ in speech-on-speech processing? Frontiers in Psychology, section Auditory Cognitive Neuroscience, in press.

Social Cognition (Case study #2)
Joke Spikman et al.

Why is this topic important? What is the challenge?
Worldwide, neurological disorders such as traumatic brain injury (TBI), stroke, brain tumors, Parkinson's disease or Huntington's disease are expected to become one of the largest causes of disease burden. For TBI alone, an estimated 69 million individuals suffer this injury each year. Behavioral problems are common in patients with moderate to severe TBI as well as in other neurological disorders. Behavioral problems include not being mindful of personal distance, difficulty in keeping up with or ending conversations, not conforming to social rules and poor anger management. Underlying building blocks for adequate behavior, referring to emotion perception, interpretative processes and regulation responses are called social cognition processes.
Social cognition focuses on the role that cognitive processes play in our social interactions. Impairments in social cognition due to various neurological disorders are common and frequently result in social behavior problems which have devastating consequences for everyday functioning of patients with these disorders.

What is needed to address this challenge? And how are you specifically addressing it?
Timely identification and treatment of these impairments are essential. However, for many years, little was known about social cognition and its importance has been neglected. In clinical practice, there was a lack of knowledge regarding how impairments in social cognition manifest themselves, how they affect everyday behavior and in which neurological patient groups they commonly occur. Only recently has social cognition been acknowledged as a crucial and full-fledged neurocognitive domain (DSM V, 2013). Prof. Joke Spikman and her group from the UMCG aimed to identify these problems in social cognition in different patient groups, translate them into research topics, and implement the results to create visible spin-off in health care, thus improving the lives of patients (and their families) with social cognitive problems that resulted from a neurological disorder such as TBI.

Introduce your research and the MAIN outcomes that benefited a certain part of society. Mention the partners and stakeholders that helped you to get there.

To kick-start this process, the group initiated strong participation in patient care in an acute setting (academic hospital) as well as in a rehabilitation setting. In close collaboration with specialists in neurology, neurosurgery and rehabilitation, they pinpointed the challenges and formulated research questions.
Through their research, they demonstrated that social cognitive and social behavioral problems are present in various groups of neurological patients (TBI, Stroke, SAH, brain tumors, Parkinson's disease, Huntington's disease, neurodegenerative disorders), that these problems interfere with adequate functioning in everyday life and that they negatively impact social participation. They developed new, validated neuropsychological tests to assess impairments in social cognition and published a new method to treat these patients, which led to the creation of a multifaceted treatment protocol for impaired social cognition and social behavior (Westerhof –Evers et al, 2019, social cognition and emotion regulation: a multifaceted treatment (T-ScEmo) for patients with traumatic brain injury. Clinical Rehabilitation 33, 820-833).

The evaluation in patients who sustained traumatic brain injury (TBI) showed that this protocol was very effective in improving social cognition and social behavior. Through collaboration with NIP (Nederlands Instituut voor psychologen, together with Prof. C. van Heugten) the group included this protocol in the Dutch National Guideline on Neuropsychological Rehabilitation. They are currently evaluating whether T-ScEmo is also effective for patients with other neurological disorders (funded by a grant from Hersenstichting Nederland, DR-2019-00317).

How was the project implemented in society? What is the effect on society? Which parties were involved in this process?
This project involved collaboration with various partners including the Brain Foundation (Hersenstichting), the Dutch Association of Neuropsychology (NVN), the Dutch Association of Rehabilitation Physicians (VRA), professionals in stroke care (landelijk kennisnetwerk CVA), the Belgian and French societies for neuropsychology, and the NIP. This ensured that the amended guidelines are used in clinical neuropsychological practice, thus enabling clinical neuropsychologists to include social cognition as a relevant neurocognitive domain in their assessments. As a result, the quality and relevance of diagnostics has improved.
Prof. Spikman and her team offer a freely available treatment protocol for social cognitive impairments that is likely to result in improvements in social cognition and behavior. They made presentations on social cognition for neuropsychologists and medical specialists, other healthcare professionals as well as for patients and the general public. They also gave workshops for clinical neuropsychologists to implement the treatment protocol. Furthermore, educate the next generation of neuropsychologists, they are giving lectures to master's students, supervising master's thesis and traineeships in on social cognition in clinical neuropsychology, and are lecturing on social cognition in the national RINO curriculum for the BIG Clinical Neuropsychologist specialism.
Through these efforts, approximately 80% of clinical neuropsychologists in the Netherlands are now familiar with social cognition as a neurocognitive domain and they understand how to assess social cognitive impairments with neuropsychological instruments (list of training programs and workshops). A substantial proportion of these clinicians have also been trained to give the social cognition treatment, which means that it can now be offered to patients in various settings (including rehabilitation).

‘No Guts No Glory’ (Case study #3) - Brain foundation anniversary prize

Iris Sommer, Sven van IJzendoorn, Hermie Harmsen, Teus van Laar, Barbara van Munster and Benno Haarman

In September 2020, a collaboration of preclinical and clinical researchers from our institute (Prof. Iris Sommer, Prof. Sven van IJzendoorn, Dr. Hermie Harmsen, Prof. Teus van Laar, Prof. Barbara van Munster and Dr. Benno Haarman) won the anniversary price of €1 million for their proposal, which was called No Guts No Glory.

The project will investigate the gastrointestinal system of patients with four brain disorders – schizophrenia, Alzheimer’s disease, Parkinson’s disease and bipolar disorder – and will assess disorder-specific gut characteristics and identify how gut abnormalities can be compensated in patient-derived innervated gut-organoids.

In a second phase, it will treat 84 patients with an anti-inflammatory diet for 3 months to optimize gut health and compare the efficacy of this intervention with diet-asusual on disability, symptoms, cognition, well-being, gut health and general health.

The phase is designed as a randomized controlled trial (RCT) with cross-over and 6-month wash-out. The diet, developed by the gastroenterology team UMCG and Wageningen University, reduces the inflammatory status of the gut. In a second trial, disorder-specific probiotics that were developed on the basis of the gut-organoid study will be given to 88 patients for 3 months in a double-blind randomized placebo-controlled cross-over design, with 6-month wash-out. Similar outcomes will be measured as in the dietary RCT.

This project will provide basic understanding of the gut-brain axis in four different brain disorders and develop two interventions to optimize gut health and improve the course of brain disorders.
We are particularly proud of this project as it clearly demonstrates the power of preclinical-clinical collaborations. Importantly, it is also a transdiagnostic study. One of the aims of our institute is to share knowledge across brain disorders and investigate whether specific underlying mechanism are shared across different disorders. This is exactly what the No Guts No Glory study will do.

‘Healing treatment-resistant depression’ (Case study #4)
Robert Schoevers et al.

1. Why is this topic important? What is the challenge?
Every year, about 850,000 people in the Netherlands suffer from depression, ranging from mild to very severe. In a small percentage of this group, about 110 people a year suffer from a non-psychotic, severe depression. At present they can only be treated with electroconvulsive therapy (electroshock therapy), which is an arduous treatment involving long hospital stays, repeated anesthesia and severe side effects that can sometimes cause permanent damage, including autobiographical memory impairment.
In the search for alternative treatments, the group of Prof. Schoevers from the department of Psychiatry of the UMCG is investigating the potential use of psychedelic substances to treat patients with mental disorders for conditions such as severe depression, addiction, posttraumatic stress disorders and end-of-life depression or anxiety.

Psychedelic substances have been used to achieve different experiences and mood states. The psychedelic experience is characterized by changes in visual perception and hallucinations, euphoria, moments of altered consciousness, so-called mystical experiences and feelings of increased connectedness with oneself and others. In the past, psychedelics such as the hallucinogen LSD (lysergic acid diethylamide) was thought to be beneficial in psychotherapeutic sessions, while mescaline was used to enhance perception, wisdom and consciousness. After 35 years of relative silence following the US drug ban in the 1970s, in the last 10 years there has been renewed interest in the potential of psychedelic substances for the treatment of patients with mental disorders.

2. What is needed to address this challenge? And how are you specifically addressing it? What is the approach you are going to take?
Current studies are focusing on the use of pharmacologically diverse substances such as serotonergic psychedelics (psilocybin, LSD, ayahuasca), serotonin-releasing drug 3,4-methyenedioxymethamphetamine (MDMA), the atypical psychedelic ibogaine and dissociative anesthetics such as the N-methyl-d-aspartate (NMDA) antagonist ketamine. All can induce alterations of conscious states, as well as a wide range of psychological, cognitive, emotional, and biological effects that may be relevant for their therapeutic effect when administered within a psychotherapeutic context. Although a range of effective psychiatric treatments are available for patients with various mental disorders, treatment resistance is a major clinical problem and there have been very few innovations in pharmacological treatment. For a drug to become a standard medicine, scrutinous testing is certainly needed, especially when used in more severely ill patients with psychiatric illnesses. Moreover, differentiating the direct pharmacological effects from the effects of the setting in which the drugs are administered is not a simple matter. In all aspects of medicine, the mindset of the patient and the therapeutic environment are important determinants of clinical outcome. This could be even more so where psychedelic compounds are concerned.

Prof. Schoevers and his group, which consists of clinical and fundamental researchers, senior faculty, PhD students and master's or bachelor's students, have initiated a placebo-controlled low-dose ketamine randomized controlled trial and a psilocybin dose-finding study, and will soon start a nationwide trial comparing the efficacy of oral esketamine to that of electroconvulsive therapy (ECT).

3. Introduce your research and the MAIN outcomes that benefited a certain part of society.
The studies conducted by Prof. Schoevers' group focus on the safety, clinical benefits and possible side effects of psychedelics, with additional research questions on the psychotherapeutic mechanisms involved. Ketamine treatment currently has the best evidence for short-term use in patients with severe, treatment-resistant depression, but these findings have been disputed, so more studies are needed. Furthermore, the possibilities for longer-term maintenance, also in terms of possible side effects and tolerance, are still unclear. Other substances such as psilocybin are in an earlier phase of research and definitely still need to demonstrate their potential in patients with more severe mental disorders. Patients included in the trials are provided with psychedelic medication in a friendly, quiet environment with soft light, music and two therapists, who the patient already knows and trusts, in continuous attendance. Such a setting, and the stepwise preparation for it, could induce significant placebo effects. In addition, the noticeable direct pharmacological effects of psychedelics often make these substances hard to 'blind' in randomized controlled trials, which also increases the risk placebo response.

4. How was the project translated and implemented in society? What is the effect on society? Which parties were involved and facilitated the process of implementation?

The results of the studies conducted by Prof. Schoevers' group will help to demonstrate whether psychedelics can be introduced safely in clinical treatment to alleviate the suffering of patients with severe mental disorders. Extensive scientific scrutiny will be applied to the research to determine the actual benefits and potential side effects. When this project is completed, registration of ketamine as an antidepressant may be applied for via the usual channels. This would also mean that the treatmentwould then be reimbursed by the health insurer – which is not the case with offthe- shelf medicines. It is quite conceivable that in a few years' time, esketamine (the left-handed enantiomer of ketamine) in one form or another will be prescribed for patients with a previously untreatable depression, will be administered by institutions and professionals and that reimbursement of the treatment costs will be possible at the individual level.

In this project, the UMCG is collaborating with several hospitals and mental healthcare institutions. The LUMC, Amsterdam UMC (location VUmc), Pro Persona (location Nijmegen) and PsyQ/Parnassia Groep Den Haag are participating, as well as the patient organization Association for Depression (Depressie Vereninging) and MIND, the umbrella organization of clients in mental healthcare. A total of four parallel studies have been made possible by funding from the Netherlands Healthcare Institute (ZorgInstituut Nederland) and the funding agency ZonMw, via the Promising Care program (Veelbelovende Zorg programma). Based on the scientific evidence, the Netherlands Healthcare Institute (ZorgInstituut Nederland) will take a position at the end of the research process within six months on whether care meets the 'state of the art' and can therefore be classified as insured care.
Also see 'The ketamine study' (https://zorgnu.avrotros.nl/uitzendingen/uitzending/item/drugs-als-medicijn-dokters-van-morgen-30-10-2018/)

‘Virtual Reality treatment for psychiatric disorders’ (Case study #5)

Wim Veling et al.

1. Why is this topic important? What is the challenge?

At the core of psychiatric disorders are problems in interacting with the world and oneself. Psychological treatments aim to improve these interactions. Patients have to experience and process a variety of interpersonal situations and practice new behavior in situations they find difficult. Conventional psychological treatments depend on the willingness and ability of patients to do this ‘homework’ between sessions, and have no control over events and situations patients encounter.

Also, psychiatric disorders like depression and anxiety are highly prevalent, and the demand for treatment exceeds the available resources. It therefore seems necessary for sustainable mental healthcare to implement technological solutions, and shift treatment to interventions requiring fewer human and financial resources by promoting self-management.

2. What is needed to address this challenge? And how are you specifically addressing it? What is the approach you are going to take?

Treatments for psychiatric disorders may become more efficient and cost-effective using Virtual Reality (VR). This technological solution provides the opportunity to create virtual situations, events and interactions that can be practiced during treatment sessions or at home. VR lowers the threshold for patients to engage in difficult situations. It enables personalized, controlled exposure and behavioral experiments. The VR Mental Health Lab at the UMCG department of Psychiatry (www.vrmentalhealth.nl) is developing novel VR treatments, investigating their efficacy and cost-effectiveness and working on implementation in mental healthcare.

3. Introduce your research and the MAIN outcomes that benefited a certain part of society.

In collaboration with software engineers, VR companies, clinicians and patients, we have developed interactive VR software systems that can be used for various psychiatric problems. We have explored the safety and validity of VR for patients with psychotic disorders. In a randomized controlled trial (RCT), we found that VR cognitive behavioral therapy (CBT) was highly effective for reducing paranoid delusions and social anxiety. As a next step, we are currently investigating the costeffectiveness of this intervention by comparing VR-based CBT with regular CBT. Other novel treatments include VR social cognition training, aggression treatment, modular VR treatment to improve social functioning in patients with psychosis, and

VR relaxation. We showed that a self-management VR relaxation tool, using 360 degrees VR videos of natural environments, immediately lowers perceived stress and improves the participants' emotional state, not only in patients with psychiatric disorders, but also in nurses working on Intensive Care Units and employees with high levels of work-related stress.

4. How was the project translated and implemented in society? What is the effect on society? Which parties were involved and facilitated the process of implementation?

We have a longstanding collaboration with CleVR, a VR company that distributes the VR treatment software in mental healthcare. More than 30 mental healthcare institutes in the Netherlands and abroad are currently working with our VR software and treatment protocols. Recently, we launched a VR start-up (VRelax) to develop and implement the VR relaxation tool in mental healthcare, hospitals and occupational medicine. We received the Prix Galien Medtech Innovation Award in recognition of this start-up, thus demonstrating both the potential and the actual progress we have made. We are working on gaining approval of insurance reimbursement for VR psychological treatment in mental healthcare in collaboration with insurers and the Dutch Healthcare Authority, and we provide courses, supervision and webinars for psychologists and other healthcare workers.