Letter to the Editors

Apparently the cover of our last edition “Heat or cold- what’s good for the brain?” caused some astonishment. What was it on the picture? Some sort of glowing brain? A jelly fish? It’s actually a brain ice cube! This little thingamajig is available in those stores that sell things no one really needs and can be purchased both online and offline. A clear must-have for neuroscientists!

Enjoy reading!

- Marietta, Editor-in-Chief

Cover: Julia Rummel
Evidence-Based Medicine: In Search of Proof for Practice

At the cornerstone of modern healthcare is a concept that has become ubiquitous in the field - evidence-based medicine (EBM). The concept of EBM - medical practice built on high-quality evidence to guide decision making - is simple, but the rationale behind it and the mechanisms by which medicine has become inherently connected to the need for `proof, proof, and more proof` are complex.

Centuries ago, doctors practiced medicine based on what they had learned from their more experienced peers. Treatments were either given to patients based on undocumented and often unreliable observations that they had worked before in similar conditions, or on logical steps linking the disease process - or what was understood of it - to the treatment.

These approaches seem reasonable, yet they disregard the fact that the human body is both complex and highly variable from person to person. Soon people realized that a single observation of treatment effect is rarely useful, since it often proves unrepeatable. Moreover, people recognized that taking `logical leaps` from science's understanding of an illness to its treatment often leads to a dead end. Numerous currently available drugs that have been proven to help relieve illness have no obvious link to the disease itself, or have a mechanism of action seemingly unrelated to the disease process.

Benefit and Risk

EBM as we know it, is a new concept that was established at the end of the last century. With a plethora of new pharmacological agents and treatment options becoming available to doctors, the importance of the above mentioned shortcomings in medical practice became more apparent. Doctors soon agreed on one guiding principle: every drug is a poison. As early as in the 19th century, Oliver Wendell Holmes, Sr. (an American physician) made a bold but accurate declaration: "I firmly believe that if the whole materia medica, as now used, could be sunk to the bottom of the sea, it would be better for mankind - and all the worse for the fishes."

Every medication prescribed, no matter how innocuous it may seem at first glance, has the potential to harm whoever uses it. Thus, in order to prescribe a drug, one essential criterion must be met; the benefit of the drug must exceed its risk. EBM aims to determine whether this is true for every diagnostic or therapeutic intervention. It does this by referring to multiple levels of evidence, each with its own level of reliability. During this process, the evidence is collected, critically analyzed for quality and dependability, and then translated into guidelines for implementation. The process doesn't stop there - it is followed by a period of thorough evaluation and continuous modification of the existing guidelines.

Evidence can be gathered from expert opinions, observational reports or from various types of research studies including randomized controlled trials (RCTs). Moreover, evidence can be acquired by grouping a large number of similar studies and analyzing them together in order to answer a specific question. Known as meta-analyses, these provide robust evidence not only due to their large size, but also due to the scrutiny that the individual studies receive. The overall appropriateness of the study design, the selection of involved subjects, the outcomes measured, and the statistical methods used are some of the factors assessed.

Shortcomings of Evidence-Based Medicine

By definition, alternative medicine is any treatment approach that has either not been subjected to the scrutiny of EBM, or that has failed to show benefit beyond its risk after undergoing this process. It's no surprise that proponents of alternative medical strategies are also supporters of the concept that benefit of any treatment must be proven to exceed risk - after all, what both sides want is to help, not harm, patients. However, they argue that EBM as is currently practiced is riddled with problems, and that alternative medical treatments are particularly prone to falling victim to these deficiencies. The reason for this is that RCTs are usually conducted in a highly restricted manner; the patients involved in the trial as well as the intervention itself are often specifically defined, with the study being optimized to avoid being influenced by additional factors. This is done to make sure that any treatment effect detected by the study is due to the treatment itself and not due to other influences, such as placebo effect. This approach is somewhat unrealistic - in practice, patients are heterogeneous; each person's illness is different from the other, and they accordingly receive different treatments optimized to their condition, often including multiple interventions simultaneously.

In alternative medicine, the primary treatment is usually coupled with various lifestyle and social changes that complete the patient's management. These factors may be neglected in RCTs, thereby reducing the chance that a treatment effect will be detected. Some people have suggested a need for more pragmatic trials, so called because they deviate from the classical methodology of clinical trials and allow for multiple interventions, including ones that are difficult to quantify precisely such as physiotherapy, psychotherapy or counselling [1].

Another issue with RCTs is that they usually compare novel interventions to placebo (an intervention similar to the treatment being tested but which has no direct biological effect). In many alternative treatment strategies such as acupuncture, producing a convincing placebo is challenging. In fact, there is much debate surrounding whether comparing any new intervention to placebo is appropriate - the placebo, by definition, produces a change (usually a positive one) in the patient's outcome. Therefore, stating that an intervention shows no effect `beyond placebo` is not necessarily the same thing as stating that it is useless.

There is no doubt that medicine has made huge progress in how it identifies and evaluates treatments over the past few centuries. However, the innumerable untreatable diseases currently in existence are proof that these methods are flawed, and more effort is needed to optimize how evidence for a potential treatment is gathered, analyzed, and interpreted. (ak)

References

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Integrative Medicine

By Prof. Dr. Andreas Michalsen, Professor for Naturopathy at the Institute of Social Medicine, Epidemiology and Health Economy, Charité Berlin and Chief Physician at the Clinic for Internal Medicine and Naturopathy, Immanuel Hospital Berlin

Complementary medicine, naturopathy and ‘whole medical systems’ (e.g. global ethnomedical systems such as Chinese medicine, Ayurveda, etc) have their origins in longstanding tradition and the empirical observation of diseases and their treatment by practicing doctors. For two decades there has been increasing scientific interest and rapidly growing evidence from clinical research in this field. Data from European and U.S. surveys consistently reveal that 40 to 70% of the population want to be additionally treated with complementary medicine methods in the case of disease. Concomitantly, it has been suggested to combine both conventional medicine and proven methods of complementary and naturopathic medicine for best patient care within the frame of ‘Integrative Medicine’ - thereby also respecting patients’ preferences. Integrative medicine has been defined by the National Institutes of Health (NIH) and the U.S. Consortium of Academic Health Centers for Integrative Medicine as “the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals, and disciplines to achieve optimal health and healing”. In Germany, naturopathy and several related fields such as acupuncture, physical therapy, manual medicine, massage, and other methods are practiced by licensed board-certified individuals with defined clinical training. According to Kneipp, integrative medicine and European naturopathy (Naturheilkunde) are based on intensive health-promoting lifestyle modifications with a focus on healthy nutrition and diet, fasting, exercise, stress reduction, mind-body medicine, hydrotherapy and thermal therapy. Here, the concept of salutogenesis, which means the emphasis on individual patient resources and the inclusion of self-help measures, support of self-efficacy, and self-healing capacities to empower patients, are important and supported by a systemic health and disease concept approach. A second concept is the hormetic stress response (hormesis), implying that low-dose physical stressors such as exercise, caloric restriction or fasting, thermal therapy or hydrotherapy induce health-promoting adaptive responses. Further modules of complementary medicine are herbal medicine (phytotherapy), osteopathy, traditional European medicine (such as leech therapy and cupping) and global traditional medicine methods such as Chinese medicine, Japanese Kampo medicine, and Indian Ayurveda medicine.

In the meantime, numerous complementary and naturopathic treatment methods have shown their efficacy in randomized clinical trials and meta-analyses. Examples are fasting therapy for rheumatoid arthritis, acupuncture in pain syndromes, leech therapy against symptomatic osteoarthritis, yoga in cardiovascular disease and back pain, meditation and bloodletting against hypertension, Mediterranean and vegetarian diets in coronary disease, hydrotherapy in heart failure, probiotics in inflammatory bowel disease and cupping in back pain. Furthermore, numerous herbs and nutritional supplements have been found effective in clinical trials, for example St. John’s wort in depression, beetroot and hibiscus tea in hypertension, rosehip in osteoarthritis, baldrian in insomnia, mistletoe in cancer and many more.

There is still controversy as to what extent placebo responses are part of the clinical effects of some complementary methods. Placebo responses are prominent in all medical treatments, regardless of conventional or complementary origin. Studies have revealed that attention, the quality of the patient-practitioner-relationship, setting factors, and the overall treatment atmosphere are important factors in increasing the total effectiveness of a healing method. In fact, complementary and naturopathic doctors spend more time with their patients than conventional doctors and have a more individually tailored approach. Furthermore, most of the complementary and naturopathic treatment methods have only minor adverse effects and are generally quite safe. This beneficial profile of complementary and naturopathic medicine may also explain the increasing demand by patients of this type of medicine. On the other hand, many complementary methods require an active and motivated patient as a partner in the care and management of their disease which is, due to lack of compliance and adherence, not always the case.

More recently the field of mind-body medicine has attracted growing interest by both the public and the scientific community. Experimental studies have described many links between stress and chronic diseases such as cancer, cardiovascular, autoimmune, and neurodegenerative disease. Numerous studies have found beneficial effects of meditation, relaxation, yoga, and other stress reduction techniques on gene expression and many relevant signal pathways. It has also become clear that stress reduction complements the lifestyle modifications necessary to fight against the epidemics of diabetes, metabolic syndrome, and chronic pain in Western societies.

In conclusion, the field of complementary and naturopathic medicine has seen a tremendous increase in scientific activity. More than 20 international PubMed-listed journals nowadays have their focus on research in complementary and naturopathic medicine. In the course of globalization and the rise of China, India, and other Asian and Arabian nations, more of their traditional complementary methods will merge into modern and science-driven complementary medicine. Future research will allow us to more precisely tailor the right method for the individual patient and to separate the wheat from the chaff.

The article is based on the following literature:
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2013 International Graduate Program Medical Neurosciences
The Placebo Effect - is it all in my Brain?

The word ‘placebo’ is most often associated with a bunch of others, be it ‘placebo-controlled study’ or ‘placebo effect’, and is now really fashionable to use. By definition, placebo is an ineffectual treatment (medicine or a simulation of a medical procedure) given to patients to deceive them. The placebo effect occurs when the patient gets significantly better – sometimes even to a level of a real treatment.

Complementary medicine often relies on therapies that do not have scientifically proven mechanisms. Previous research showed that conditions treated most often by unconventional medicine, for example, back pain, fatigue, allergies, asthma, depression, arthritis or anxiety, are the ones that present an inordinately strong placebo response [1]. Therefore, it is speculated that the placebo effect plays a big role in complementary medicine treatments. According to Kaptchuk, the placebo effect is not just a dummy intervention, but also comprises other factors, such as the patient-physician relationship, nature of the illness, or the setting [1]. Alternative medicine involves treatments that pave a certain amount of mystery and show effects that can highly influence the placebo effect and that are almost never offered by conventional medicine. Acupuncture involves a sensation of vital energy flowing through our bodies, chiropractors release audible sounds that influence our body, and psychic healers use tingling vibrations [1]. On the other hand, mainstream medicine mostly comprises passive treatments or administration of medication, which does not increase the placebo effect to a huge extent.

When You Believe

In a study from 1964, three groups of patients were given pills with an embedded magnet and told that they were acting either as relaxants, stimulants or placebos. After investigation of gastric motility in the patients, it appeared that the pill worked according to what they were told [1]. Another study showed that sham acupuncture procedure had the same (positive) effect on patients with chronic cervical osteoarthritis as true acupuncture or diazepam (the patients were blinded) [2]. An additional disease entity that is very prone to the placebo effect is depression. Clinical studies of antidepressants showed that, in some cases, it is impossible to distinguish the placebo effect from the effect of the active drug. It is said that 75% of the effectiveness of antidepressants is actually due to the placebo effect [1]. Scientists claim that the degree of the placebo effect depends on the power of belief.

Neuroscience of the Placebo Effect

The concept is interesting and sometimes surprising, yet you may wonder how it all works. How can our mind influence our body? Studies performed on patients with Parkinson's disease showed that placebo could induce higher release of dopamine in the dorsal striatum, thus producing an improvement in the patients' symptoms (24% as opposed to 30% in the conventional treatment) [3]. Increase of dopamine release was also observed in the ventral striatum, which is associated with motivation and reward anticipation. The authors therefore concluded that this mechanism is necessary (yet not sufficient) for the placebo effect to occur. Wager and colleagues showed that placebo in analgesia works by potentiation of endogenous opioid responses to noxious stimuli [4], an effect that can be blocked directly by opioid receptor antagonists [3]. It is supposed to be mediated by brain structures such as the periaqueductal gray matter (directly related to pain responses), dorsal raphe nuclei, amygdala and the anterior cingulate and lateral prefrontal cortices. Another study showed dopamine release in the nucleus accumbens after administering placebo to patients for pain treatment [5]. It is suggested that the opioid system in the placebo response is engaged by expectations driven by the prefrontal cortex [3], which cooperates with the reward system and involves dopamine release in certain brain structures.

Placebo vs. Nocebo

Since the mechanisms of a number of complementary medical procedures are still not known, we are entitled to think that the main mechanism here - if not the only - is the placebo effect. However, researchers are not so forward in presenting their opinions. Most of them claim that the placebo effect plays an important role in unconventional medicine, yet it is not the only basis for the beneficial effects. One must realize that the placebo effect is a positive experience and requires not only information that a certain procedure will be effective, but also many other aspects such as: attention, compassion, and attitudes of the practitioners themselves. Answering the question ‘Is it all in my brain?’ requires considering another important effect - the nocebo effect - which is exactly the opposite of the placebo effect. Studies showed that verbal information suggesting intensification of pain after administration of an inert drug caused increased pain, by means of increasing cholecystokinin release - an opioid antagonist [5]. We can therefore claim that the brain has a huge effect on our body that we should never underestimate.

References

PhD Thesis Award

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Excellent PhD theses are awarded with the Deutscher Studienpreis. The PhD thesis has to have been defended in 2013 with magna or summa cum laude at a German university or, for German citizens, at a university abroad. Deadline for submission: March 01, 2014. Further information: http://www.koerber-stiftung.de/wissenschaft/deutscher-studienpreis.html.

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Research on Researchers

Dr. Michael Teut

In this issue, we would like to introduce Dr. Michael Teut who does clinical research about the effects of traditional, alternative or complementary therapies and works as a physician at the Institute of Social Medicine, Epidemiology and Health Economics, Charité Universitätsmedizin Berlin.

MZ: What is your academic background?
MT: I was trained as a physician, mainly in Internal Medicine, Geriatrics, Family Medicine, Hypnotherapy and Complementary and Alternative Medicine. Since 2007, I have been working as researcher and physician at the Institute of Social Medicine, Epidemiology and Health Economics, Charité Universitätsmedizin Berlin.

You studied in the Netherlands and in India. What did you experience there?
Both countries have completely different cultures. In 1994, I spent a few months of clinical training in a homeopathic hospital and college in Mumbai. India's medical system is split into three parts: conventional medicine, ayurveda, and homeopathy. Approximately 250,000 Indian physicians work as homeopaths and are running hospitals and clinics. I personally wanted to study this phenomenon more closely and subjectively had the impression that, in many cases, homeopathy produced good results, but in others, conventional medicine was clearly superior. This experience helped to support my decision to pursue Integrative Medicine, which combines the best therapeutic strategies from different systems to optimize health care for individual patients with individual needs.

In the Netherlands, I participated in a four-month surgical internship at the Leiden University Medical Center, which was very good training. Practical bedside teaching was of utmost importance and I participated in many operations and worked frequently in the emergency unit. Teamwork was clearly very important, and was a strength of the Dutch colleagues.

What do you do in your current position?
Together with my colleagues, I was able to set up the Charité Outpatient Department for Integrative Medicine at Berlin Mitte (Charité Hochschulambulanz für Naturheilkunde), which provides outpa-
tient care and conducts clinical trials. I am also teaching medical students in Social Medicine, Prevention, Health Economics and Complementary and Alternative Medicine. At the moment, we are running clinical trials on the effects of mindful walking and cupping in chronic low back pain and ‘Kneipp’ therapies in elderly patients in nursing homes.

What are your main topics of interest in science?
I am mainly interested in clinical research about the effects of traditional, alternative or complementary therapies. If you enter this field, placebo discussions will automatically arise. In the last years, I became more and more interested in ‘self healing’. In clinical research, the term ‘placebo’ is frequently used. But placebo is a ‘black box’, the meaning depends on the context in which the term is used. In my understanding, one important aspect of ‘placebo’ is self healing and conditions which support self healing. Already the school of Hippocrates in ancient Greece advised lifestyle changes to increase self healing, to improve health, and support healthy aging. Much of the ancient advice remains true today. Although we know about the benefits of lifestyle change, modern medicine is mainly focused on technical solutions. Therefore, I consider trials that investigate the effects of simple and low-tech lifestyle change interventions to be of high importance. Good examples are our trials about the effects of mindful walking exercises on psychologically distressed subjects or patients with chronic back pain.

What do you think is the main advantage of integrative medicine compared to conventional medicine?
Over the last years, I realized that integrating traditional therapies in conventional medicine enables physicians to use a wider range of metaphors and concepts to help patients to create meaning about their complaints and disease. This can help the patient to reframe his situation, reduce distress, and also activate resources for self healing. Physicians integrating traditional therapies usually spend more time with their patients. Time is a crucial resource to medical quality: to understand patients, build up a good patient-physician relationship, also to avoid errors. In addition, many traditional therapies have low side effects and can be tried before, after or in combination with conventional treatments.

How will medicine look like in 20 years from now?
Medical progress is strongly driven by new technologies and industry. Introducing new technologies confronts us with great opportunities but also risks. I hope that we will be able to master this challenge and our patients may benefit from technical advances. In the United States, Integrative Medicine has become a very strong movement. Nearly all academic centers are now running departments for Integrative Medicine. The US government strongly supports scientific research in this field with more than 100 million dollars per year. I personally understand this movement as a counterbalance to the technologically driven medical progress. I hope that creating evidence for traditional therapies may lead to an integration of useful strategies in conventional medicine in the long run.

What impressed or astonished you most during your career?
The tendency of many physicians and journalists to generally classify complementary and alternative medicines as ‘placebo’ and conventional medicine as ‘effective’. Both sides are part of our medicine culture. Placebo responses occur in both systems and play essential roles in both. Conventional medical practice, as practiced in real life, is in many cases not evidence-based. We should generally be more open minded, curious, but also critical towards all therapeutic strategies.

Thank you very much, Dr. Teut, for this intriguing insight into your work and life. (mz)
**What else can Be Helpful for our Unhappy Brain?**

By Tian Zhang, PhD Student Medical Neurosciences, AG Clinical Neurosciences

Contrary to complementary medicine, which is combined with conventional treatment, alternative medicine is used in place of conventional medicine. Using a special diet to treat cancer instead of undergoing surgery or chemotherapy is a good example of an alternative therapy [1]. Within alternative medicine, many systems built upon distinct theories and practices exist. While in Western cultures homeopathic medicine and naturopathic medicine are common, traditional Chinese medicine (TCM) and Ayurveda are the two most popular systems in oriental cultures.

The use of alternative medicine is higher among patients with chronic conditions, especially when conventional treatment is ineffective. Since neurological diseases are often chronic and challenging to treat, alternative medicine is a constant attraction for patients suffering from a wide spectrum of neurological conditions, such as back pain, sciatica, memory loss, or migraine. On the other hand, research regarding the efficacy of utilizing alternative medicine in neurological conditions has been promising. Evidence is emerging for alternative interventions in back pain management - a meta-analysis of acupuncture for low back pain concluded that acupuncture is effective for short-term relief of chronic pain [2].

Herbal and nutritional therapies are one of the essential elements in alternative medicine. However, not enough studies with suitable sample sizes and adequate control groups have been done to screen the efficacy and safety of all compounds that have been taken by patients. For example, Ginkgo has anti-platelet effects that could cause unnecessary bleeding in stroke patients or interact with anticoagulants [4]. Case reports of some herbs suggest pro-convulsive effects [5]. Therefore, caution should always be taken when deciding whether to substitute conventional medicine with alternative therapies.

In summary, alternative medicine is commonly used by patients with chronic neurological conditions, and can help in most cases of disease prevention and treatment. Nevertheless, further research is still needed to investigate how alternative medicine can alleviate neurological symptoms and to evaluate how alternative therapies may benefit the large population seeking to make their brain feel better.

**References**


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**Holistic Healing - Homeopathy**

By Dr. Damera Srinivas, MVSc, Veterinary officer Madras Race Club, Guindy Chennai

Alternative medicine is a system of treatment of diseases followed around the world, since only one system of medicine may not be able to cure everything. Homeopathy is one such example. The aim of homeopathy is to cure an illness by treating the whole person rather than merely concentrating on a set of symptoms. Hence, in homeopathy the approach is holistic and the overall state of health of the patient - especially their emotional and psychological well-being - is regarded as significant.

A homeopath not only notes the symptoms that the person wishes to have cured, but also takes into account other signs of disorder that the patient may regard less important. This is because illness is a sign of imbalance within the body. A homeopathic remedy must be suitable both for the symptoms and the character and temperament of the patient. Therefore, two patients with the same illness can be offered different remedies according to their individual natures. Similarly, the same remedy can be used to treat different symptoms in different people.

Homeopathic remedies are based on the concept that ‘like cures like’, an ancient philosophy that can be traced back to the 5th century BC. It was discovered by the German doctor Samuel Hahnemann in the 1800s who believed that the existing medical practices were too harsh and hindered rather than aided healing. He found homeopathy useful for treating diseases without causing the side effects of allopathic medicine.

Dr. Hahnemann discovered that quinine, an extract of the cinchona bark, used for the treatment of malaria, produced symptoms of the disease when taken in a small dose by a healthy person. The production of symptoms was the body’s way of combating illness. Thus, to give a minute dose of a substance that simulated the symptoms of an illness in a healthy person could be used as a way of fighting it.

Modern homeopathy is based on extracts derived from plant, mineral and animal sources and used in extremely dilute amounts. The curative properties are enhanced by each dilution as impurities that might cause unwanted side effects are lost. However, the scientific community remains skeptical about the curative effects of homeopathy although some clinical trials have produced positive results [1, 2]. In general, it helps to be open towards all kinds of therapy as they all have the same aim- to relieve the patient from distress.

**References**

The Healing Power of Self Control

The connections between mind and body have long been known. However, scientific evidence for the control of the brain over the body emerged only in the early 20th century. Therapeutic applications based on this knowledge include progressive muscle relaxation [1] and autonomic training [2].

Biofeedback as an official term, model, and technique came to use in 1969 [3] and stands for the awareness of physiological processes using instruments. It combines psychology, neurophysiology, cybernetics, and medicine. Reflection of the physiological status of one’s own body enhances the control over oneself. Acknowledged regulation of bodily reactions can reduce the frequency or severity of disease attacks. Therapeutically relevant physiological parameters used in the biofeedback approach include: temperature, skin sensitivity, muscle tone, lung and heart function, and brain activity [4].

Biofeedback was first investigated for the treatment of neurotic complaints and hypertension. With time and increasing knowledge, biofeedback has been successfully introduced for many more clinical indications. Nowadays, the technique is part of the therapy regimens for illnesses such as: pain-related diseases (tension-type headache, migraine, and chronic pain), substance abuse, epilepsy, Raynaud’s disease, hypertension, nocturnal enuresis, and incontinence [3,5].

Increased control over one’s physiology enables one to also control disease better. Biofeedback is able to provide long-lasting effects and minimal, if any, side effects. This makes biofeedback invaluable for managing disease attacks in chronic – especially neurologic - conditions for which effective medications are lacking or poorly tolerated.

Evidence about the harmful effects of chronic medication intake has prepared a fertile surface for the development of biofeedback, which might be the solution for some conditions that are difficult to manage with conventional medicine. (cr)

References

Meditation - The Art of Healing
A Short Expose of the Use of Meditative Practices in Clinical Setting

By Nikolas Karalis, PhD Student, Centre for Integrative Neuroscience, Tübingen

Meditation is a general term referring to a set of practices centered on the training of the mind and the regulation of attention and awareness. The roots of some of these practices go back to the history of man and the first religious ceremonies.

In the contemporary era, meditation is practiced both in the religious context (spanning practically every type of religion) and in the secular context, either as an effort to attain well-being in a constantly accelerating world or with clear therapeutic intentions. The ability to induce altered states of consciousness with the meditative practice is exploited in various treatments, to heal both the body and the mind. Mindful breathing, progressive muscle relaxation, attention meditation, and loving kindness meditation are just some of the categories of meditative practices, named after the main characteristics of the technique and taken out of spiritual context. The main behavioral components of meditation are described as relaxation, concentration, an altered state of awareness, a suspension of logical thought and the maintenance of a self-observing attitude. Different combinations of meditation and other types of therapies - such as cognitive behavioral therapy and neurofeedback - have been successfully used for treating patients with anxiety, chronic stress disorders, post-traumatic stress disorder, depression, chronic pain, attention-deficit hyperactivity disorder and other emotion-related disorders.

Although there are clear benefits from the practice of different meditation techniques, there is still a general lack of understanding of the neurophysiological mechanisms underlying these effects. Consequently, the practice of meditation in clinical settings is still not very wide. However, a growing body of evidence on the positive effects and mechanisms of action helps integrate these techniques in everyday clinical practice.

For a concise review on the neurophysiological correlates of meditation and its clinical applications, see [1] and [2].

References

Source: http://commons.wikimedia.org/wiki/File:Yoga_Meditation_Pos-410px.png
Autogenic Training or the Power of Self-Suggestion
By Anne Schwerk, PhD Medical Neurosciences, AG Neuronal Regeneration and Plasticity

Autogenic training is one of the most well-known relaxation techniques and was developed by Prof. Johannes Schultz and Wolfgang Luthe in 1932 in Berlin. Their inspiration came from the neuroscientist Dr. Oskar Vogt, who found that it was possible to reach a hypnotic state without relying on external suggestions but purely on the self.

Schultz aimed to develop a method that rendered the patient responsible and independent of the hypnotist. Hence the name autos (self) and genos (creation). The underlying principle is based on ‘selective awareness’ through autosuggestion in order to reach a higher level of self-regulation and relaxation. Such selective awareness is reached by focusing on self-suggestions and internal physiological processes, e.g. the regulation of blood flow to specific body parts and instructing these parts to become warm and heavy. While applying this technique, emotional responses and physical sensations can be triggered and released. This sort of self-regulatory training is most effective when the individual is highly motivated and receptive to instructions and suggestions. Furthermore, the individual must maintain a strong sense of concentration and body awareness, meaning that the technique may not be suitable for all. Still, autogenic training – apart from sharpening one’s focus and mind control – is used for a broad variety of conditions, such as insomnia, hypertension, tension headaches, migraines, bronchial asthma, and for certain types of pain disorders [1,2].

Even though autogenic training is the most frequently used relaxation method in German-speaking countries, there is only little consistent evidence for its effectiveness, with many studies lacking rigor and quality when reviewed [3]. One big meta-analysis [1] showed medium to large effect sizes in clinical studies that are stable at follow-up and that exceed placebo effects. Another meta-analysis showed that autogenic training is effective, but less than meditation in reducing anxiety over ten years [4]. Hence, it seems to be an appropriate tool for many psychosomatic disorders, though not more than unguided techniques such as meditation.

References

Hypnotherapy in Action
By Harald Krutiak, Psychological Psychotherapist, Appointee for Teaching and Research at the Charité

Have you ever experienced meeting someone familiar on the street but cannot remember when or where you met them? And much later, perhaps when you are about to fall asleep, the answer comes into your mind all by itself?

This shift from: ‘I do’ to ‘it happens’ is exactly what hypnotherapists use trance for. Hypnosis in contemporary understanding is characterized by two main points: first, the focusing of attention and second, the shift from active searching to allowing mental processes to happen by themselves. Contemporary hypnosis is a very natural, everyday state; we go into trance several times a day. For example, on the highway, we are often so absorbed by thoughts that we do not always remember the last 100 kilometers we drove. This ability to go into trance by ourselves is also the reason why hypnotherapists do not necessarily induce a so-called formal trance, but just create en-passant using specific patterns of communication, this delicate state. Therefore, hypnotherapy can be regarded as an art of communication. As each individual responds in their own personal way to trance, hypnotherapists create an environment to support the client that is perfectly suited for each person. Thus, every trance is unique!

This is also what I really love about working with hypnosis. It is a fantastic and challenging method of therapy. I also appreciate the fact that I do not have to have a ready solution for the patient, but just support them by creating an altered state of consciousness, so that the solution can develop by itself. At the same time, hypnosis opens the door between the mind and the body. This explains why going into a trance improves health, solves somatic problems, and activates the enormous power of self healing processes.

For me, originally coming from a background of psychoanalysis (as I am from Vienna, this is self evident), the work with trance is a fantastic tool that not only creates insight, as analysis does, but is also a highly potent way of creating changes. Hypnosis is in that understanding also part of early therapeutic methods, we find it in shamanism and other traditions of healing.

May the power of this long history be with me!
Nature as a Toolbox for Drugs in Neuroscience and Beyond

One of the most difficult steps in developing a drug to treat an illness is finding a biological target for the compound to act on. In many cases, nature has solved this problem for us, and all it takes are a few astute observations from people to figure out how we can make use of our surroundings to improve and maintain our health. Once the effects of a certain plant or animal product on the human body are observed, the exact substance causing these effects must be extracted. Pharmaceutical chemists then synthesize these compounds or compounds closely related to them as a potential drug that undergoes further safety and effectiveness testing.

In areas of the world where malaria is endemic, quinine is one of the most effective treatments for this parasitic infection. Now reserved for the most severe cases of malaria, this drug has been used for centuries in South America and Europe to treat fever and shivering. Quinine is an alkaloid (compounds containing basic nitrogen atoms) derived from the bark of the cinchona tree, and possesses the characteristic bitter taste of this plant. Reserpine, another alkaloid, is a drug used to treat hypertension and psychosis. Although not commonly used nowadays, it remains an option for treating those with high blood pressure who are resistant to other medications. The compound was first isolated from the Indian snakeroot Rauvolfia serpentine. This plant also contains another chemical - yohimbine - which acts on the alpha 2 receptors of adrenaline and is used as a remedy for erectile dysfunction.

The willow tree (genus Salix) has provided humanity with one of the most important drugs we have ever used. The plant contains the active compound salicin, used for centuries to relieve pain and fever by Native Americans as well as the Ancient Egyptians. In fact, salicin was the drug at the center of the first clinical trial in scientific history, conducted in 1763 [1]. In the late 1800s, it was used for the production of acetylsalicylic acid (Aspirin) - the most widely used drug in history, which single-handedly converted Friedrich Bayer's company from a small dye manufacturer to a pharmaceutical titan. The cardiac glycoside digoxin is extracted from Digitalis lanata (foxglove). Early attempts at medicinal use of this plant were hindered by its toxicity and fatality in overdose. It currently has an important role in the treatment of heart failure as well as abnormal rhythmicity of the heart, yet requires stringent monitoring and careful dosage prescription to avoid its harmful effects.

The aptly named plant Atropa belladonna was once used by women in Italy to dilate their pupils and make them look more attractive. It contains a mixture of toxic alkaloids (known to cause hallucinations) that inhibit the action of the autonomic nervous system (the part of the nervous system devoted to controlling the automatic, unconscious functions of the body). Derived from this plant is the widely used anticholinergic drug atropine, which is used in ophthalmology to dilate the pupils, to treat cases of organophosphate (insecticide) poisoning, and to treat those with abnormally low heart rates. Another anticholinergic drug, curare, acts on a distinct set of receptors and was once widely used as a muscle relaxant during anaesthesia. Derived from the Strychnos toxifera plant, this paralyzing poison was historically used by South American tribes to cover the tips of their hunting arrows.

Angiotensin-converting enzyme (ACE) inhibitors were derived in the 1960s from the venom of the Brazilian pit viper, Bothrops jararaca. The venom kills by causing a severe drop in arterial pressure through blockage of the renin angiotensin aldosterone system, an essential physiological mechanism which controls blood pressure. ACE inhibitors such as lisinopril, captopril and enalapril have become first-line agents for high blood pressure, particularly in younger Caucasian patients, and have a good safety profile. It is noteworthy that their selective mechanism of action means that ACE inhibitors may not be effective for everyone in terms of lowering blood pressure. Despite this, the drugs have several other unique benefits including protecting the kidneys in diabetes and improving heart function in patients with heart failure [2].

A more recent drug yielded from nature’s gift basket is exenatide, an anti-diabetic agent licensed for use in 2005. This drug was isolated from lizard (Gila monster) saliva and has been shown to stimulate insulin release from the pancreas [3]. Unlike other anti-diabetic drugs, exenatide has an important feature - it only increases insulin secretion when glucose levels are high and therefore, does not lead to an abnormally low blood glucose (hypoglycaemia). It also has numerous other beneficial effects including promoting weight loss. Similarly, a new agent proposed for the treatment of stroke is also derived from saliva - that of the vampire bat Desmodus rotundus. This drug, called desmoteplase, is still in the testing phases of development (phase III trials), but has already shown great promise [4]. It stays in the body for a longer time than other thrombolytics (drugs which dissolve blood clots), is more selective in its action, and does not lead to neurotoxicity. It is possible that it may represent a breakthrough in the treatment of stroke, which is currently a highly debated and complicated issue.

Nowadays, we are in possession of complex methods to design, test and use medicines. Despite this, it’s not uncommon that a drug crosses our path which reminds us that no matter how technologically advanced we are, our dependence on nature is eternal. People have been using the earth’s natural resources for medicinal purposes for millennia, and continue to do so. However, only a handful of these substances - which include both animal and plant products - have been scientifically deemed safe and effective enough for modern use. (ak)

References
[1] Stone, Philos Trans, 1763
Green Tea and its Extracts for Healthy Brains

Bettina Schmerl, MSc Student Medical Neurosciences

The second most popular beverage after water, consumed either hot or cold, is prepared from brewing the leaves of Camellia sinensis: green tea. Different from the equally popular black tea, the fermentation of the leaves is prevented, retaining the eponymous original green color [1].

For a long time, consuming green tea was associated with longevity and increased health, and indeed, green tea was shown to contain the highest concentrations of different polyphenols (flavonoids, catechins, caffeine, theanine, theobromine, theophylline, phenolic acids) as well as antioxidants (epigallocatechin gallate, catechin, epicatechin gallate, gallicatechin, and epicatechin gallate), all of which were shown to be associated with health benefits [2].

A multitude of studies, mainly performed in Asian countries where the plant is cultivated and drinking green tea has a tradition of almost 5000 years [3], reported the health benefits of green tea consumption in various diseases ranging from atherosclerosis, high cholesterol, diabetes, obesity, liver and bowel pathologies to almost all types of cancers [1,4]. In many different types of brain and peripheral nerve tumors, green tea and its extracts were found to inhibit cancer cell growth and render them more vulnerable to chemotherapy and radiotherapy while simultaneously sparing normal brain cells [5,6].

Prof. Hunstein, a former internist and hematologist, provided a very intriguing self-report on the application of green tea in disease. He suffered from the rare condition lambda light-chain amyloidosis. Whilst the common therapeutic approach was rather ineffective, daily consumption of 1.5 to 2 liters of green tea per day reduced his symptoms substantially [7].

Meta-analyses of studies investigating the effects of daily green tea consumption reveal that there are major variations in the daily intake, concentration, and preparation methods of green tea, and have not found definite proof of clinically relevant benefits [1]. However, more recent studies have relied on chemically pure green tea extracts, more specifically epigallocatechin-3-gallate (EGCG).

This compound was shown to be beneficial for the central nervous system. Since green tea is associated with healthy aging, researchers investigated its effects in diseases of the elderly: Alzheimer's and Parkinson's disease.

In vitro and in vivo models, similar to Prof. Hunstein's amyloidosis report, showed that EGCG decreases A-beta plaque burden by inhibiting peptide aggregation and promoting production of non-cytotoxic peptides through the modulation of secretase activity [8,9]. Additionally, green tea extract acts as an anti-inflammatory compound, scavenging free radicals and promoting hippocampal neurogenesis, all of which are beneficial in Parkinson's disease [10]. The extract does not only prevent cognitive decline by slowing down neurodegenerative processes, but was found to improve cognition even in healthy brains [11]. In small animal as well as human studies, researchers found evidence for the psychological relevance of green tea and its extracts. Reports indicate that green tea reduces stress and even has an antidepressant-like activity [12,13].

Moreover, there is evidence that EGCG prevents cognitive deficits after stroke, in Huntington's disease and Down syndrome patients [14-16]. Another very promising trial - which was recently performed here at the Charité - investigated the anti-inflammatory actions of EGCG in multiple sclerosis (MS), an autoimmune disease with unknown origin that causes CNS damage by attacking the myelin sheath and causing inflammation and neuronal death [17]. Previous research groups, now present on the Charité campus, had found that EGCG strongly reduces symptoms in the EAE mouse model of MS. The green tea extract is a neuroprotectant and reduced general neuroinflammatory activity [18]. Regarding the now completed clinical trial, project leader Dr. Judith Bellmann-Strobl stated: “We currently evaluate the results of the SuniMS trial. We are about to unblind the data and only then will we know the effects. So far, I can only say that the investigational product was very well tolerated even at relatively high dosages.”

In conclusion, green tea consumption is very likely beneficial for the body, soul and disease prevention. However, treating individual diseases may require chemically pure compounds found in green tea extracts, which seem to exert few, if any, side effects. It appears that a healthy lifestyle is not only about veggies and exercise; have some green tea to pamper your brain!

Reference:
[10] Lee, Neurosignals, 2005
[16] De la Torre, Mol Nutr Food Res, 2013
Venoms are nature’s most deadly weapons allowing small animals to immobilize or kill foes several times their size. Their potency is now used in medicine.

Venoms consist of a complex mixture of short peptides and enzyme-like complexes suspended in a fibrous protein matrix [1]. Early attempts at using venom as a medicine failed because the raw venom was highly allergenic. Although the initial treatment showed promising effects, subsequent therapy was consequently impossible. This changed in the 1940s when Dr. Waldemar Diesing developed a method to reduce the allergic carrier protein content from around 85% to below 2%, making the active components of the venom available for therapy; The Horvi-Enzyme Therapy was born [2].

Since the 1950s, scientists have rediscovered the medical properties of venom and applied it to increasingly diverse diseases. “The dose makes the poison” is a wisdom of toxicology stating that everything (even water) is a poison if administered to a biological system in sufficient concentration [3]. Conversely, a dose of the same substance can be beneficial, if administered below toxic or fatal levels.

W.E. “Bill” Haast, an US serpentologist, scientist, and man of many talents picked up on this when he opened his Miami Serpentarium in 1946 [4]. Haast observed that in the process of a large-scale governmental antidote production, horses developed an immunity to the venoms. Considering his increasing contact with snakes, Haast figured he needed a similar immunity. He proved his idea by self-administering venom injections weekly starting at the age of 38, subsequently surviving over 172 snake bites, saving 21 snake-bite victims by donating his blood, and living a disease-free and active life [4]. Bill Haast looked and moved like a 60-year old before he died at a proud age of 100. In his long career, Haast observed that cobra venom caused the same symptoms as polio. He thus experimented on 10 monkeys by injecting them with a concentrate of the polio virus, 5 of which he also gave cobra venom. Only those with both the venom and the virus survived. Subsequently, he developed a cobra venom-based medicine that could reverse the symptoms of polio years before a vaccine was invented. Haast also invented PROVen, a viper venom-based medicine that was used to treat around 7000 patients suffering from arthritis and multiple sclerosis in the 1970s before the FDA closed down the only clinic offering the therapy and banned the drug due to insufficient clinical testing [5].

How venom-based medicine works is not fully understood. The toxin complex (from 32 snakes and one salamander species in Haast’s case) might simply train the immune system to swiftly destroy any invading pathogens and support homeostasis. Venoms represent a hyper-specialized weapon that has been evolved and upgraded by thousands of animals [1]. The short peptides and protein complexes attack several systems of the body by mimicking active wild-type compounds in those systems. Most often, venoms attack the same system by several routes and more than one system at once [1]. These inherent capabilities may lead to the development of a novel class of drugs, which slow aging, prevent infections and autoimmune diseases. Many more applications for venoms are still being discovered.

The author of this article does not take responsibility for injuries resulting from handling venoms and advises “Do not try this at home (or anywhere else)! You might not survive it.”

References

Contest
We are always interested in including your contributions. You can submit anything you see fit on the topic of neuroscience. Send us your most exciting microscopic pictures, or a creative photo, thoughts on neuroscience or self-written poems – whatever comes to mind! The best contribution will be published and rewarded with the book “Advice to a Young Scientist”. So, what are you waiting for? Start the engine of your mind and get going! Trust us, it is worth participating! Send your contribution to cns-newsletter@charite.de to win the Medical Neurosciences shoulder bag.
Deadline for submission for the next issue: January 31, 2013.
This issue’s winner is Nikolas Karalis who contributed two articles to this issue: “Meditation – The Art of Healing” and the conference report on the Bernstein Conference 2013. Thank you very much for your contribution.
It is widely believed that colors (defined as electromagnetic radiation in the visible range) can influence our physiology. Interior designers would recommend a yellowish home office, as it enhances concentration, and a reddish kitchen for appetite stimulation. If the hypothesis that colors can influence our physiology is valid, it is not far to think that colors could also have the potential to heal.

As early as 2000 BC people used colored stones, crystals and salves to heal wounds [1]. Since then, several postulations about the impact of colors have been made (e.g. Acivenna, Babbitt [1]). Collectively, they characterize the color red as activating, blue and green as soothing, and yellow as anti-inflammatory [1]. Dinshaw Ghadiali extended this approach with the principle that particular areas of the body (chakras) respond to particular colors. In his Spectro-Chrome encyclopedia (1933), he concluded that every element would correspond to a certain prismatic color and that a disease would reflect an imbalance. This was based on the phenomenon that heated elements had a specific emission spectrum. Thus, a specific pathology could be treated using the appropriate color [2]. Other color therapists have extended his work (e.g. Klotsche, Takkata, Ott [1]) and reported beneficial effects on various pathologies [3]. The results of all these publications sound plausible in the context that different wavelengths have different properties. But they all have one common feature that questions the efficacy of color therapy: the lack of scientific evidence. Current evidence for the efficacy of chromotherapy consists of case reports [3], small trials or studies utilizing full-spectrum light instead of applying distinct colors (e.g. Takkata, see [1]). While some associations may be based on evolution (e.g. red arouses attraction), others are contextual and individual [4].

In conclusion, robust scientific correlations between pathology progression and color application are still missing. So, if you think that you recover best from a cold by lying on a red sofa wrapped in a yellow blanket, stick with it. However, if you are diabetic you should probably stick to conventional insulin therapy rather than follow Ghadiali’s advice of exposing yourself to yellow and magenta!

References
[2] Spectro-Chrome Therapy, JAMA 1935

Figure adapted from vectorcharacters.net

Chromotherapy - Colorful Nonsense?
By Betty Jurek, PhD Student German Center for Neurodegenerative Diseases

Oppenheim-Preis 2014
The Deutsche Dystonie-Gesellschaft awards excellent clinical and basic research in the area of dystonia with the Oppenheim-Preis 2014 (5000€). Contributions about the etiology, pathogenesis, diagnosis and therapy of dystonia as well as the psychosocial situation of the concerned are wanted, particularly from scientists below the age of 40. More information: http://www.dystonie.de/die-ddg/oppenheim-preis.html
Simply Put, Music Can Heal

By Tian Zhang, PhD Student Medical Neurosciences, AG Clinical Neurosciences

The idea of using music to heal has been postulated as early as in the writings of Aristotle and Plato. The first recorded music therapy intervention was in the 1800s in an institutional setting (Blackwell’s Island in New York). Interest in music therapy continued to gain support thereafter. By definition, music therapy is the evidence-based clinical use of music interventions to accomplish individualized therapeutic goals by a credentialed professional who has completed an approved music therapy program [1].

Modern music therapy consists of two main domains. One traditional working area is psychiatric music therapy, where music is used as a tool of self-expression and interaction. Another traditional domain is music therapy for developmental and neurological disorders. While psychiatric music therapy is often based on a relatively free and spontaneous working paradigm, music therapy for developmental and neurological diseases is more structured and method-oriented [2].

It is hard to find anyone who does not like music at all. Vast differences exist only when we talk about emotions different music can arouse or personal experiences that have been attached. Since the majority of psychiatric disorders are associated with emotional disorders, it is no wonder that music has been useful to regulate emotion. Fortunately, experiences with emotional entities and interaction become possible with music therapy even when verbal expression is absent, which is the case with infants, people with dementia, or patients suffering from acute psychosis. Music therapy, however, is not limited to listening; actively playing an instrument can also be rewarding for body coordination and motor function of patients with motor disabilities. Finally, it is often not only the music but also the relationship between the patient and the therapist that makes the therapy work.

To sum up, music therapy is one of the most important complementary therapies and can be applied to various diseases. Music therapy research is also an active area [3-5], which greatly promotes the development and new applications of music therapy in both psychiatric and neurological clinical settings. Isn’t it nice that we can both enjoy music and be healed at the same time?

References

Bernstein Conference 2013

By Nikolas Karalis, PhD Student, Centre for Integrative Neuroscience, Tübingen

The ninth installment of the annual Bernstein Conference for Computational Neuroscience, organized by the Bernstein Center for Computational Neuroscience Tübingen, took place from September 24-28, 2013 in Tübingen attracting 550 participants.

Two days before the official kick-off of the conference, a series of pre-conference workshops took place, featuring specialized talks and open discussions on a range of hot topics in experimental and computational neuroscience such as spatial navigation, calcium imaging, neural computation, and others.

The main axes of the conference revolved around cortical dynamics and circuits, the physiology of vision, computational vision, and decision-making. The program included many exciting talks from some of the leading computational neuroscientists from Europe and abroad. The list of invited lecturers comprised Drs. A. Movshon, E. Simoncelli, M. Usrey, P. Roelfsema, A. Pasupathy, R. Rosenholtz, A. Torralba, P. Perona, D. Fitzpatrick, N. Rochefort, A. Renart, A. Karpova, and A. Kepecs. These lectures were complemented by very interesting contributed talks, a total of 80, as well as 250 poster presentations over two poster sessions, spanning a wide range of topics within computational neuroscience.

During the conference, Dr. Hermann Cuntz from the Ernst Strüngmann Institute (ESI) for Neuroscience was awarded the Bernstein Award 2013 – a prize worth 1.25 Million Euros over 5 years - for his work with morphological modeling. Dr. Cuntz investigates the effects of shape and morphology of nerve cells on the structure and function of neuronal circuits.

In addition to the academic program, a Science Slam open for the general public took place, and the public was also invited to watch and vote for the short films participating in the Neurovision Film Contest 2013.

During the weekend following the conference, the PhD Symposium took place, asking the question “How many brains do we need to understand the brain?”. The PhD Symposium consisted of social get-togethers for Master and PhD students as well as talks by Andrea Burgalossi, Catherine Cutts, Matthew Larkum, and Abigail Morisson.

The Bernstein Conference 2014 will take place from September 2-6, 2014 in Göttingen. The official program as well as the abstracts of the oral talks and posters presented this year can be found on the official website of the conference.

More information
www.bernstein-conference.de
Once upon a TiMe

A long time ago at a hospital for elderly people with psychiatric disorders, I entered one of the rooms to check on an Alzheimer’s disease (AD) patient who had been recently admitted. In a small room with two beds, one next to a window overlooking a small garden and another on the other side of the room, I slowly entered and stood facing one of the beds and the window behind. It was a bright day with the sun hiding behind a few passing clouds. I instantly remembered my childhood and my family. A day on the beach or barbecuing in a park, just the scene from the window was sufficient to take me away to that memory until she said, “Mom, mom”. The patient lying in front of me had started calling. I quietly listened to her as she looked at me and at the window. “Mom,” she said, “where is the food? Mom, can we eat breakfast outside? Mom” she kept calling out repeatedly. At that moment, I felt myself in another scene; a little girl standing next to her mother in a small kitchen with a small window above the sink and a small wooden dining table nearby. A plant or perhaps a few half-dying flowers stood in a vase on the table. Even though I had my own past onto which I reflected, my patient had been re-living hers again with no sense of present. Time and memory had failed her; she was now in a world that I wished would bring her more peace than the war that she had been constantly fighting with AD.

A German-Swiss polymath known by the name Paracelsus once said: “Time is a brisk wind, for each hour it brings something new. But who can understand and measure its sharp breadth, its mystery and its design?” So, what is time? How do we perceive time? And though the answers have been debated for many years, it is no hidden fact that time, whatever and wherever it is, shapes our lives.

Throughout many years, experiments on time and time perception have been carried out by psychologists. Fraisse says that the notion of time comprises two concepts; 1) the concept of succession in which two or more events are perceived as different and sequential and 2) the concept of duration which represents an interval between two successive events. And thus, as he notes, it is when the perception of duration is conjoined with the perception of succession of events that the notion of time develops [1]. Friedman beautifully outlines how this succession is the basis of our learning and understanding of the world. In his book, he argues that even though time is perceived on the basis of successive events (e.g. A - B), the world does not appear to us as a flow of accidental and arbitrary occurrences. Yet, it appears to us as occurring in an orderly and organized pattern. For humans to perceive the world this way, they must understand the process of cause and effect (e.g. AàB) and hence, must recognize temporally discrete events [2]. Such a process allows us to perceive a world that is coherent and meaningful.

In fact, not only is time important in creating a comprehensive world but it is also important in learning. Experiments were performed on preschoolers where they were asked to relate between temporally contiguous yet inconsistent events and consistent but temporally non-contiguous events show that they are able to connect the former. Such an experiment meant that preschoolers relied on temporal cues in cause-effect relations. This outlines that temporal cues are used as a learning process in children until they acquire more knowledge and rely on other methods as well. The perception of duration and succession is present early during childhood, but only when they are integrated at the age of 7 or 8 is the notion of time developed.

So how do we perceive time? Some have proposed that the underlying mechanism of experienced time is a pacemaker accumulator clock producing a series of pulses – ticking like a clock. The number of pulses recorded then represent the duration experienced. The recorded pulses are then compared to units of pulses stored in long-term memory. The more experiences you record, the longer the time it seems to acquire. When you remember your childhood, you feel as though each experience in it was very long compared to adult experiences. This is because children record new memories and this increase in memory-encoding leads to an increase in the duration of the perceived time [3].

The space-time dimension has been created with the creation of the universe. Time controls our lives in many ways; from the circadian clock to other physiological mechanisms, and even in the existence of our universe from the big bang to the creation of galaxies – everything involves time. So where is it in our brains? Areas ranging from the right prefrontal cortex, basal ganglia, and posterior parietal cortex to the cerebellum have all been found involved in time perception [3]. It was then proposed that time perception depends on distributed, modality-specific, and time-keeping processes that might then converge onto the posterior parietal cortex. Yet, it is not only a structure-dependent function but an unsteady and changing one. Like Einstein had charmingly phrased it: “When a man sits with a pretty girl for an hour, it seems like a minute. But let him sit on a hot stove for a minute – then, it’s longer than any hour. That’s relativism!” Likewise, time perception depends on emotions. If you are bored or depressed, time seems to flow very slowly, sometimes painfully so. When anxious or fearful, time seems to speed up. An explanation for this phenomenon was that increased or decreased attention and arousal could affect the rate of the internal pacemaker clock and thus change our perception of time.

Some physicists assume that the universe had to be created in this specific manner for us to perceive it. Its characteristics had to be conceivable to our minds. Perhaps similarly, time also had to be created in this specific manner for us to perceive it. Therefore, time might be an inherent component of our existence as we might also be. Time is a contracting and dilating dimension of the universe as much as it is in our minds despite the different factors involved. Whether or not we agree on the actual directionality of time, we seem to perceive it as directional and differentiate between today, yesterday, and tomorrow. And the stories of our lives always begin with: once upon a time. (ys)

References

www.medical-neurosciences.de
# German Courses in Berlin

<table>
<thead>
<tr>
<th>Institution</th>
<th>German Level</th>
<th>Duration</th>
<th>Class Size</th>
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<td>Individual learning online</td>
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<td>Berlitz Sprachschule</td>
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<td>• Individual courses: min. 10 lessons</td>
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<td></td>
<td>• Intensive courses: 6 lessons/week for 10 weeks</td>
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<tr>
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<td></td>
<td>• Daytime intensive classes 5x3.5h/week</td>
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<td>• Individual courses or private courses (e.g. with a friend): minimum of 10 lessons</td>
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<td>• One month intensive course (4 hours/day) in September and March</td>
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“Price is relatively cheap, however the quality of the teachers are rather questionable, small rooms. Crowd: prep school students, young people.” – Ferry Sagala

“Difficult to get in, must book really early. Rather for advanced levels (starting from B1). Great quality, Great teachers. Cheap.” – Ferry Sagala
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<td>- €42+/45min for individual lessons</td>
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<td>- between €45+/45min and €54+/45min for 2 to 8 people in total</td>
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<td>- evening classes (4-8 participants) 4 weeks 16x45min €169, 8 weeks 32x45min €299</td>
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<td>- intensive course €145 for 1 week, €275 for 2 weeks, etc.</td>
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<td>- Individual courses: €44/45min</td>
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<td>- Intensive courses: €840 + €147 for learning material</td>
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<td>- €205/course (plus one course book per month of around €20 new, but sometimes you can buy it used from other students)</td>
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<td>- Intensive courses: €840 + €147 for learning material</td>
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</tr>
<tr>
<td>- €205/course (plus one course book per month of around €20 new, but sometimes you can buy it used from other students)</td>
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<tr>
<td>- €619 for standard courses</td>
<td></td>
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<tr>
<td>- €59/45 min for individual lessons</td>
<td></td>
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<tr>
<td>- €39/45 min for classes with 2-3 participants</td>
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<tr>
<td>- €29/45 min for classes with 4-8 participants</td>
<td></td>
</tr>
<tr>
<td>- Morning classes €234/month, afternoon/evening classes €198/month</td>
<td></td>
</tr>
<tr>
<td>- €40/semester</td>
<td></td>
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<tr>
<td>- €400/Intensive course</td>
<td></td>
</tr>
</tbody>
</table>

“Very positive. I studied here for 6 months straight (B1.2-C2.1), and my German improved so much because of it. The price for the course is really fair and I think you really get your money's worth. But, you have to be motivated to study at home in your spare time, otherwise you won't really gain much from it.” – Anna Schröder

“I took a B1.2 class. The class was small and great for learning. I spoke and interacted a lot. The quality was great, grammar was spot on. The teacher was friendly, and I think what is taught is controlled. My experience is very similar to Goethe Institut but for a much lower price.” – Niraja Ramesh

“Great teachers, I would recommend for the basic levels (until B1) to do it here. Really expensive, but think of it as an investment, because it will give you a good foundation for the advanced levels. If you are serious about mastering the language, start here. Crowd: serious students, companies, embassies.” – Ferry Sagala

“Teachers were very experienced, class size wasn't too big. The workload is very light but I think it's perfect for people with a busy schedule.” – Ahmed Khalili
<table>
<thead>
<tr>
<th>Institution</th>
<th>German level</th>
<th>Duration</th>
<th>Class Size</th>
<th>Costs</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inlingua</td>
<td>All levels</td>
<td></td>
<td>- Individual courses: min. 10 lessons - Combi-10: 20 lessons in groups, 10 individual lessons - Evening classes: 1 or 2x2 lessons - Daily classes: 20 lessons/week - Saturday classes: 3 lessons for 10 weeks</td>
<td></td>
<td><a href="http://www.inlingua-berlin.de/sprachenlernen/deutsch.html/">http://www.inlingua-berlin.de/sprachenlernen/deutsch.html/</a></td>
</tr>
<tr>
<td>Sprachenatelier</td>
<td>All levels</td>
<td>1 month and then more if you want</td>
<td>max. of 10 in a class, currently in my class we are 5</td>
<td>€100 for 4 weeks or €190 for 8 weeks</td>
<td><a href="http://www.sprachenatelier-berlin.de/">http://www.sprachenatelier-berlin.de/</a></td>
</tr>
<tr>
<td>Sprach- und Kulturbörse der TU Berlin</td>
<td>All levels</td>
<td>2 blocks of 6-8 weeks during the semester, 3, 6 or 9h/week</td>
<td>10-15 participants</td>
<td>€112 for 60x45min, €149 for 80x45min</td>
<td><a href="http://www.skb.tu-berlin.de/contao/index.php/en/">http://www.skb.tu-berlin.de/contao/index.php/en/</a></td>
</tr>
<tr>
<td>Volkshochschule</td>
<td>All levels</td>
<td>Different possibilities, e.g. twice a week, everyday, usual length: 100x45 min</td>
<td>10-20 participants</td>
<td>€150 for 100x45 min</td>
<td><a href="http://www.berlin.de/vhs/kurse/deutsch/deutschfremd.html">http://www.berlin.de/vhs/kurse/deutsch/deutschfremd.html</a></td>
</tr>
<tr>
<td>Zentraleinrichtung Moderne Sprachen (TU Berlin)</td>
<td>A1-C1</td>
<td>One semester, 1x or 2x/week (2-4h/lesson)</td>
<td>Not known</td>
<td>€48/semester</td>
<td><a href="http://www.zems.tu-berlin.de/">http://www.zems.tu-berlin.de/</a></td>
</tr>
<tr>
<td>Zentraleinrichtung Sprachenzentrum (FU Berlin)</td>
<td>A2-C1</td>
<td>One semester, 1x or 2x/week (2h/lesson)</td>
<td>Not known</td>
<td>Not known</td>
<td><a href="http://www.sprachenzentrum.fu-berlin.de/">http://www.sprachenzentrum.fu-berlin.de/</a></td>
</tr>
</tbody>
</table>

Course fees were investigated in October 2013. No fee guarantee. (mz)
Neuroscience in Your Everyday Life

Is it True that People Born in Summer Need Less Sleep than People Born in Winter?

Why do some people seem to need less sleep than others? Why is it so easy for some people to get up in the morning and for others it’s easier to stay up late at night?

As far as we know, there is no data on the association between sleep patterns and birth dates. I even asked an expert on the topic: Prof. Dr. Till Rönneberg from LMU Munich. However, he told me that this has not been investigated in depth. What has been thoroughly investigated though is why some people are early birds and some are night owls. This has to do with our inner clock that has evolved to help us anticipate the daily changes in our environment, such as light-dark cycles or temperature cycles. Almost everyone’s inner clock is happily ticking away with an approximately 24-hour period (that is why it is termed ‘circadian clock’ – circa dias = almost a day). However, the ticking speed varies. Imagine you have a fast inner clock. This means that you would be too early for everything: you wake up early, eat early and get tired early; you would be an early bird, or as the scientific community terms it – an early chronotype. The opposite is also true; late chronotypes have a slow inner clock, so they are ‘late’ for everything.

The interesting thing is that our chronotype varies throughout our life; we all start off as very early chronotypes, our clocks become gradually slower until the end of puberty and then getting earlier again during the rest of our lives. Not only is our chronotype age-dependent, but also sex-dependent.

These differences in individual chronotypes are definitely something which we have to keep in mind when discussing school hours or office hours. These are often much too early especially for school children in the midst of puberty.

Last but not least, I want to mention an important feature of our inner clock, and that is that it is able to synchronize to our environment through light. This means that it can entrain the 24-hour day-night cycle provided it receives enough light input. To cut it short, the more light we get, the easier it is for night owls to get up in the morning and the longer early birds can stay up at night.

Reference
All Information was taken from: Rönneberg and Merrow, Cold Spring Harb Symp Quant Biol, 2007

Do you also sometimes wonder about the simple neuroscientific questions in everyday life, but don’t really feel like looking them up right away? For questions like this, just mail us your question (cns-newsletter@charite.de) and Dr. Harebrained will give us his explanation in the next issue!

Our next issue’s question: Why is it again that we have ‘déjà vu’ experiences?

13th Berlin Summer School “Psychiatry as a Science and as a Profession”

The 13th Berlin summer school “Psychiatry as a science and as a profession” was a fun-filled intense educational week that took place in the last week of August, attended by over 17 psychiatrists and students from 13 different countries: a truly international setting!

The school was organized by Prof. Dr. Norman Sartorius, Prof. Dr. Andreas Stroehle, and Prof. Dr. Andreas Heinz. Prof. Sartorius has been described as one of the most prominent psychiatrists of his generation and, despite his impressive qualifications, is the least bit intimidating and will surprise you with his agility and memory!

The week started on a Sunday evening, with the participants introducing their countries of origin. During the week, we were involved in several practical demonstrations of essential tools starting with how to make introductions, presentation, and poster techniques, how to participate in discussions, and how to write proposals. After each practical session, Prof. Sartorius presented the essence of the topic and the take-home messages in the form of short presentations. Learning by doing thus seemed to be the motto of the Summer School.

Most importantly, we also learned the art of constructive criticism - a very valuable skill. It was obvious that the professors were familiar with the saying: “all work and no play makes Jack a dull boy”, as the mentally stimulating mornings and afternoon sessions were nicely balanced with a good number of social events in the evening - which included a tour of the city and a boat ride on the Spree. The summer school concluded with Prof. Sartorius handing out diplomas to the participants and practical advice about the priorities in our lives. It was definitely an honor to be taught by him and I certainly recommend taking part in the school. Last but not least, the summer school resulted in some lasting friendships because it consisted of a perfect number of participants: it was neither too big nor too small.

Applications for next year’s Summer School begin in March. Watch out!! (arm)
THREE-YEAR DOCTORATE IN INTERDISCIPLINARY MIND AND BRAIN RESEARCH

APPLY FOR DOCTORATE IN INTERDISCIPLINARY MIND AND BRAIN RESEARCH:
perception • decision-making • language • brain disorders and mental dysfunction • plasticity and lifespan • philosophy of mind & ethics • human sociality and the brain

FURTHER INFORMATION
www.mind-and-brain.de

APPLICATION DEADLINE
15 January 2014
Positions for PhD and Master Students in Neuroscience Research in Berlin

Type: Lab Rotation/Master Thesis
Title: Expression, function and endogenous modulators of transient receptor potential channels TRPV1, TRPV6 and TRPM8 in uveal melanoma (UM)
Field of Research: Role of TRPs in very malignant tumor cells using highly sensitive functional assays such as fluorescence calcium imaging and planar patch-clamping.
Starting Date: February 2014
Research Group: Experimental Ophthalmology, AG Stefan Mergler
Contact: Stefan Mergler, stefan.mergler@charite.de, tel.: 030 450 559648

Type: Lab Rotation with Possibility of Extension to a Master Internship
Project Title: Identification of proteins interacting with neurotransmitter receptors and their role in brain development
Field of Research: Molecular and cellular neurobiology and brain development
Possible Starting Date/Deadline for Application: Possible starting date end of November, beginning of December, but the position will be open until it is successfully filled.
Research Group: AG Schmitz
Contact: Dr. Nutabi Camargo, postdoctoral researcher, nutabi.camargo@charite.de, tel.: 030 450 539004

Type: Lab Rotation/Master Thesis
Title: Expression, function and endogenous modulators of transient receptor potential (TRP) channels TRPM2 and TRPV6 in human corneal endothelial cells (HCEC)
Field of Research: Cell vitality and Ca2+ regulation of HCEC in context with keratoplasticity and storage of donor corneas. Highly sensitive functional assays such as fluorescence calcium imaging and planar patch-clamping will be used. Focus on TRPM2 and TRPV6.
Starting Date: Immediately
Research Group: Experimental Ophthalmology, AG Stefan Mergler
Contact: Stefan Mergler, stefan.mergler@charite.de, tel.: 030 450 55964

Type: Master Thesis Project
Title: NDRG1 - a mediator of glioma angiogenesis and glioma growth
Field of Research: Neurooncology
Starting Date: Immediately
Research Group: Experimental Neurosurgery, Prof. Peter Vajkoczy
Contact: Thomas Broggini, thomas.broggini@charite.de, tel.: 030 450 536298

Type: Master Thesis Project
Title: Correlation between cognitive decline and viscoelasticity changes in the adult brain in the course of Alzheimer’s disease
Field of Research: animal study on a mouse model for AD, behavioral testing, histology
Possible starting date/deadline for application: starting date Jan/Feb 2014, application until Dec 15th, 2013
Research Group: AG Barbara Steiner, Neural Regeneration and Plasticity
Contact: PD Dr. med. Barbara Steiner, barbara.steiner@charite.de, tel.: 030 450 517295

Type: Master Thesis Project/Lab Rotation
Project Title: Mesenchymal stem cells in a hemiparkinson rat model
Field of Research: Stem cells, parkinson, regeneration, and plasticity
Possible Starting Date/Deadline for Application: As soon as possible
Research Group: AG Barbara Steiner, Neural Regeneration and Plasticity
Contact: Anne Schwerk, anne.schwerk@charite.de, tel.: 030 450 517295

Type: Lab Rotation/Master Thesis
Title: Behavioral and neurochemical effects of Deep Brain Stimulation in animal models of psychiatric disorders
(applied methods: surgery, behavioral testing incl. intracranical self-stimulation, immunohistochemistry)
Field of Research: Deep Brain Stimulation as a potential treatment for therapy-resistant psychiatric disorders
Starting Date: Immediately
Research Group: AG Christine Winter, Experimental Psychiatry
Contact: Julia Rummel, julia.rummel@charite.de, tel.: 030 450 525016

Type: Master Thesis
Title: Influence of the EphrinB2-EphB4 system on vascular resistance during antiangiogenic glioma treatment
Field of Research: Neurooncology
Starting Date: Immediately
Research Group: Experimental Neurosurgery, Prof. Peter Vajkoczy
Contact: Thomas Broggini, thomas.broggini@charite.de, tel.: 030 450 536298
I take the decaffeinated, fat free coffee. No sugar, please!

And we get the cream-filled cupcake with chocolate icing!

For the last ten issues, Benedikt has given the CNS newsletter a facelift. With almost 50 illustrations and cartoons, he has enriched a tremendous amount of articles making it so much more fun to read the newsletter. On this jubilee, we are sad to tell you that Benedikt will leave our team as he moves on in his career as a postdoc at Harvard! We congratulate Benedikt and wish him all the best for his future. Always leave them wanting more ...
Aktiv für Ihre Gesundheit
Machen Sie’s wie Magdalena Neuner und halten Sie sich mit Bewegung fit. Die TK-Leistungen unterstützen Sie dabei. Zum Beispiel:

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„Wer sich bewegt, gewinnt!“

Magdalena Neuner, erfolgreichste Biathletin aller Zeiten
Welcome 2013 Master Students
We warmly welcome the new students to our MedNeuro family from all around the world. We wish them the best of luck for the upcoming year or semester, depending on the track they have chosen. With just three students from Germany, this cohort emphasizes the ‘international’ in our program’s name.

Call for NeuroCure PhD Fellowships
Like last year, NeuroCure will offer scholarships for PhD students. The deadline for application is January 10, 2014. Details on: http://www.neurocure.de/phd-fellowships.html

Humboldt Research Track Scholarships
The Humboldt Research Track funding line is designed to support 24 outstanding Master students per year in taking a first step towards a PhD. The program offers funding for the transition phase between the end of a Master program and the beginning of PhD-level research. Applications start on December 1, 2014. Details on: http://bit.ly/lcswprU.

New Members of the Examination and Admission Committee
We also warmly welcome the new members of the examination and admission committee (ZuPrüA), Professors Friedeman Paul and Seija Lehnardt.

Christmas Party
We plan to have a Christmas party not only to get into the mood of Christmas time, but also to celebrate the end of the block lectures. The party will take place on Wednesday, December 18. We will keep you posted.

Imprint
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