From the Annals of Neuroscience: Phrenology

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Searching for Artificial Consciousness: Ex Machina and the Post-Turing Test

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Picture a Scientist: Three scientists, a global story

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For most of us, the last two years have been both standing still and running. To help ourselves reorient in time, we take a look back—and forward to both the history and future of neuroscience.

One interesting thought one may entertain when lost in one’s mind and thinking about the past and the future is to take anything you are interested in—and may take for granted—and pose the following question: was it discovered or was it invented? It may sound strange at the first moment, but it may be quite a fun game. For instance, one may think that computers were obviously invented. However, computations are more complex to determine. Assuming a computer computes mathematical operations, one may then beg the question: what about mathematics? Was it discovered or invented? And medicine? That is a tricky one, right? Do we discover cures and diseases, but we invent medications—and sometimes even some diseases... Do you see where I am going? Well, neuroscience is no different. We didn’t invent the brain, albeit the gigantic efforts of AI and robotics to recreate cognition, human or otherwise (pg. 19).

When we look back, we usually look at the tipping points: when discoveries trigger inventions. When we look forward, we imagine inventions that will lead to discoveries. And somehow in neuroscience and otherwise that is how progress is achieved. Sometimes one hypothesis leads to one bad discovery, such as phrenology (pg. 4), but its fundamental insight leads to new technologies and developments. In other cases, it seems to be an age-old tug-of-war between two hypotheses. Take the good-old nature-nurture discussion: is it the case of a simple and pure deterministic naturalism or a by-the-book genetic lottery? Could it be possible that epigenetics may play the middle man between these two opposing forces? Possibly none of these, or all of them (pg. 11). Historically, the party line has oscillated depending on the stream of the current scientific endeavor.

Science, after all, is not an isolated or objective point. Science itself comes from somewhere and leads somewhere else: a pendulum that swings from one discovery-fueled technology to the next, leading always from one hypothesis to the next, rarely failing to change the perspective on best scientific practices or models. We review one initiative, The Human Brain Project, which was expected to revolutionize neuroscience models (pg. 8). Instead of one immense innovation, sometimes one smaller breakthrough can unravel a new set of possibilities. Take for example the invention of penicillin—or rather, the discovery of penicillin’s antibiotic effects. Taken by itself, penicillin was a great success, but it also pushed the pharmacological industries into new ground (pg. 17). Sometimes the new technologies are groundbreaking only in that they enable more efficient solutions. Such is for X-ray use, which is no longer the method of choice to look into the brain, but was the precursor to stronger and more sensitive methods (pg. 6). Sometimes entire fields can be discovered—or invented?—if only the right tools can be harnessed. It is no secret that evolving genetic technologies have uncovered new genes and gene functions as well as overhauled how we investigate and even treat some diseases (pg. 9).

Technologies are not the only parts of neuroscience that change. So do the ways in which we evaluate new developments, as we question both the ethics and the effectiveness of clinical trials (pg. 15). Scientists change too. What do you see when you Picture a Scientist (pg. 21)? What about when you picture science itself? You might be surprised at what science can look like (pg. 22). We hope you enjoy discovering as much as we did, and that, hopefully, may lead us towards some new inventions.

Your Editors-in-Chief,

Bettina, Lorena and Leandre
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Phrenology is one of the many doctrines emerging from the history of neuroscience that came into disfavor. While it gripped society with fervor when first introduced, and getting your head examined to find out more about your character and personality was in vogue, we now have a much more nuanced approach towards studying and understanding the brain. Nevertheless, phrenology was an important landmark in the road to where we are today, and it is worth retracing our steps for a further examination.

**What is Phrenology?**
Phrenology, now heavily regarded as pseudoscience, was a doctrine advanced by Franz Joseph Gall in the late 1790s which stated that measurements of the surface of the skull, reflecting the localized brain function beneath, could predict mental traits.

At this time, the brain was already beginning to be regarded as „the exclusive instrument of all sensation, all thought, and all will“ [1], but Gall put forth and attempted to systematically and empirically explore the idea that „each particular faculty of [the] understanding is provided in the brain with an organ proper to itself“ [2], with the skull being representative of this underlying organization through its topography.

While we today know this by the popular term ‘Phrenology’, it was christened as such after the fact by English naturalist and physician T. I. M. Forster in 1815. When Gall originally proposed it, he referred to it as ‘Schaedellehre’ (Doctrine of the Skull), ‘Organologie’, and then simply as the physiology of the brain [3].

**Origins of Phrenology: How did it start?**
Franz Joseph Gall studied medicine at the University of Strasbourg and completed his medical degree in Vienna. He believed that the philosophical questions of human nature could be answered by looking to nature and natural consistencies [3]. He came to believe the notion that brain functions (or faculties, as he referred to them) were localized within different areas of the brain, and that these faculties had observable physical manifestations. This idea was fueled by his observation as a student that those of his classmates who were good at memorization also had larger eyes. In his words: “I could not think that with so many individuals a good memory and protruding eyes only coincidentally coincided. I surmised that there must be a connection between memory and such prominent eyes. By manifold consideration of this I had the idea: if memory betrays itself through an external trait, should not other mental qualities be externally recognizable” [4].

He set out to develop a list of these faculties as well as the corresponding brain area. The size and shape of each area could, in his view, predict the extent of the faculty the person would exhibit. Accordingly, a person’s skull would match the shape of the brain, and thus studying the topography of the skull would allow him to uncover the faculties and characteristics of the brain beneath.

Gall soon amassed a collection of 300 human skulls and 120 plaster casts [3]. He attempted to seek out the skulls of those who displayed prominent characteristics such as bravery or cold-blooded murder in hopes to decipher which brain region gave rise to these behaviors, and which skull shape was its indicator. In the end, he believed there to be 27 main faculties, each of which could be localized to a particular region of the brain and could be measured based on the surface of the person’s skull.

**The Historical Importance of Phrenology**
Today phrenology is by and large classed as pseudoscience, and the notion that the shape of a person’s skull could determine their personality, abilities, and defining traits has been repeatedly disproven. In fact, even in the 1800s, this was doubted: the Austrian government had ordered Gall to stop lecturing, and when he attempted to relocate to Paris and propagate his ideas there, they were pronounced to be scientifically invalid [2].

However, Phrenology played an important part in the history of neuroscience as Gall was able to proliferate the idea of functional localization within the brain.

Attributed to Edward Hull; Wellcome Library | Wikimedia Commons
While he was not the first to have advanced this approach (Charles Bonnet being a significant scientist to do so prior), much credit for the popularization of this concept can be attributed to him [5]. Phrenology’s fall into disfavor did not mean all the associated ideas were left behind, and though many scientists following after Gall rejected most of the basic tenets of phrenology (especially that of skull shape predicting character and ability), the idea of localization of function within the brain remained. This led to much research on patients with lesions in specific areas in order to observe which impairments would follow. The important discoveries of Broca’s area by Paul Broca (where a lesion would lead to an impairment in speech production) followed later by the discovery of Wernicke’s area (responsible for speech comprehension) clearly represent this.

It is also important to note that, at this time, many identified the head as the seat of rationality and placed emotions elsewhere. However, Gall placed emphasis on both cognitive and emotional functions arising from the brain. He also advocated that the cerebral cortex must be the area from which the most complex of higher cognitive functions emerge, given the fact that those animals considered less intelligent had nervous systems consisting mostly of a spinal cord with a much less developed brain, while those considered more sophisticated had larger and more developed cortices. This was a novel thought for the time.

The proposal of Gall’s doctrine led to a great amount of scientific activity to be carried out around the topic, leading to a strengthening of science around the brain. Gall conducted his brain dissections in a way that would allow anatomy to be viewed with great precision and accuracy, and thus contributed a great deal to the field of neuroanatomy [6]. Additionally, much activity took place in opposing Gall’s views: his largest opponent, French scientist Flourens, attempted to systematically disprove Gall’s theories. His experiments led him to find that the brain acted as a whole and not in discrete units. When damage occurred to one area, the other parts were able to take over and retain the previous functionality. This was an important finding and one which was pushed by this debate [2].

One final important role that phrenology played was that although it had many adverse social implications (discussed below), there were few domains in which it had a positive effect. For example, an idea stemming from later phrenological thinking was that of the brain being able to be manipulated or reformed. This led some to advocate for, for example, rehabilitation rather than harsh punishments for criminals. It allowed for more nuanced differentiation between those who were mentally ill and for more adequate sentences for them. In fact, one Italian psychiatrist, Biagio Miraglia, proposed a renewed classification of mental illness, basing it on brain function, which could be seen as a precursor to our modern-day classification systems such as the DSM and RDoC [7].

**Phrenology and Current Day Neuroscience**

Those who dabble in current day neuroscience will be well aware of the widespread functionality of brain regions. A heavy emphasis is laid upon the interaction of brain regions in order to produce complex networks of behavior, rather than what they do on their own.

However, phrenology allowed for a great progression in the scientific research of the time, and also gave rise to some important concepts that remain with us today. One such idea is that of the brain as an organ that could be changed through practice. Phrenologists likened the brain to a muscle which could be trained, and this idea is not at all too dissimilar from our current day understandings of neural plasticity, with the concept that training in a particular area can not only strengthen our abilities in that particular area but also change the density of certain brain regions. One popular example of this could be the famous London Taxi Drivers study, where those who had trained extensively for the London taxi driver test and had spent many years learning the streets of London had greater hippocampal volume [8].

**The Dark Side of Phrenology**

For those looking for a way to magnify the already present biases that proliferated society and science at the time, phrenology was a gift served upon a platter. Phrenology no doubt contributed to a reinforcement of already existing biases by providing adequate ‘justification’ for them. The doctrine was readily accepted in Victorian England, where it was used to justify the ongoing colonial conquests [3].

Some scientists used the concept of phrenology in order to compare the skulls of different ethnic groups and rank them from ‘most civilized’ to least. One follower of Gall believed that certain races would never be able to become ‘civilized’ due to a lack of certain cerebral features. The misuse did not stop there. Phrenology also provided an adequate rationale to further propagate the notion of gender differences between the sexes [9].

Interestingly, many modern phrases in English can trace their roots to phrenology. Now used as an adjective to describe something intellectual, ‘highbrow’ was once a descriptor coming from phrenology, where those with higher foreheads were believed to be more intelligent. Similarly, the common term ‘well rounded’ can also trace its origins back to phrenology, for having a well-rounded skull meant you were balanced in all your different faculties.

**Looking Forward**

Although phrenology can be regarded as a wrong turn in the history of attempts towards an understanding of the brain, one with the ability to be weaponized and used in problematic ways, it did constitute an important
Opening the Black-Box
For decades, researchers and physicians have tried to uncover the functioning and mysteries of our brain. The development and continuous improvement of neuroimaging were crucial for this process, as it enabled us to take a look inside the brain and slowly open this black box. Improvements in imaging technologies gave us knowledge about the structure, connectivity, and function of the brain without having to open the skull.

Introduction of X-Rays
The history of neuroimaging is still a recent one. In 1895 Wilhelm Röntgen was the first person to non-invasively collect an image of the inner human body [1]. His famous first X-Ray depicts the hand of his wife wearing a ring. As Röntgen waived his option to patent the technology, it quickly spread around the world and became one of the leading diagnostic tools for pulmonary tuberculosis, for example. Making its way into daily life, X-Rays were also used by shoemakers to assess the fit of a shoe or to remove unwanted facial hair. Back then X-Rays were very time-consuming and little was known about the negative, carcinogenic side-effects of the technology.

The First Images of the Brain
In 1912, Arthur Schüler published a book on radiology of the head, thereby describing the first study on intracranial pathologies using radiography [1]. The utility of these images however was still limited, showing only abnormalities of the bones or calcification of the tissue. Radiographic images were criticized as not being able to show abnormalities of the soft tissue or showing abnormalities only at a very late stage of disease when surgical intervention was not possible anymore. In contrast, a case series by neurosurgeon Walter Dandy in 1916 [2] was able to show radiographic abnormalities in 45% of brain tumor patients.

Improving image contrast
In 1918, Walter Dandy introduced Ventriculography as an advancement of simple radiography [1]. The technology required drilling a hole in the skull of patients to remove liquor from the ventricles and replace it with air as a contrast agent. This led to an improvement in the contrast of images and, for example, an increase in the detection rate of brain tumors by a third.

Pneumoencephalography as State-of-the-Art
Coincidentally, Dandy observed that the injected air sometimes leaked from the ventricles into the subarachnoid space leading to the development of Pneumoencephalography a year later [1]. As the subarachnoid space surrounds the whole brain, this significantly enhanced the contrast in the images and improved the differentiation of brain tissue. This procedure was later refined to remove cerebrospinal flu-
id from the spine by performing a lumbar puncture instead of accessing the brain directly. Consequently, pneumoencephalography was the state-of-the-art neuroimaging technology for the following 50 years. Yet, the technology was again associated with severe side effects such as headaches, fever, or meningitis. Mortality rates ranged from 0.6% to 30% depending on the performing neurosurgeon.

A Revolution of Neuroimaging

In 1972, the first patient was examined with a novel technology called computed tomography (CT) [1,3]. The technology was the result of a series of inventions by neurologist William Oldendorf, physicist Allan Cormack and electrical engineer Geoffrey Hounsfield. The latter two received a Nobel Prize for their works in 1979. The basis of the technology was the detection of small variations in the absorption of X-Rays depending on different tissues. In the beginning, the resulting “image” showed these absorption coefficients as numbers. Later on, those numbers were transferred into greyscale pixelated images, subsequently leading to the CT images we still know today. In the beginning, the resulting “image” showed these absorption coefficients as numbers. Later on, those numbers were transferred into greyscale pixelated images, subsequently leading to the CT images we still know today. While early CT images provided a rather bad resolution and processing could take several hours, a whole-brain CT scan can nowadays be done within seconds. Still, the beginning of CT marked a drastic change in neuroimaging. For the first time, grey and white matter could be examined non-invasively. Diseases could be identified more reliably and new conditions such as haemorrhage, oedema, or necrosis were suddenly visible in imaging. Finally, the era of CT ended more dangerous procedures such as Pneumoencephalography.

The Onset of Magnetic Resonance Imaging

One of the latest developments in neuroimaging is Magnetic Resonance Imaging (MRI), with the first human MRI scan being performed in 1977 [1]. Before this point, MRI had been tested in animals for several years and improvements in scanning times and resolution were made. The basis of MRI is a strong magnetic field as well as additional electromagnetic fields modifying the spin of hydrogen atoms. Depending on the tissue composition, different relaxation times are observed after an electromagnetic pulse. This information can then be used to create an image.

Neuroimaging as We Know it Today

MRI is still continuously being advanced. Using stronger magnetic fields, higher resolution images can be obtained. At the same time, improvements in scanning parameters lead to shortened scanning times. Different modalities of MRI imaging have been developed to improve the detection of pathologies or advance research possibilities. These developments include diffusion-weighted imaging, which allows visualization of fibre bundles in the brain, or functional MRI to study brain activity, to name a few. With advancements in virtual and augmented reality, a focus is also placed on combining different imaging modalities. In neurosurgery, for instance, fibre bundles can be overlaid on structural MRI scans to improve preoperative planning. The same fibre bundles can also be projected on the actual brain during surgery using augmented reality. Other ways to integrate these technologies are currently being explored [4].

The future

If we look at the times between important developments in neuroimaging methods, we see a major discovery occurring roughly every 40-50 years. More than 40 years have already passed since the introduction of MRI. Is it then the time for the next “world-changing” technology? The question is, what will it be and how will it change again our understanding of the brain?

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“Fibre bundles can be projected on the brain using augmented reality.”


“X-rays were also used by shoemakers to assess the fit of a shoe or to remove unwanted facial hair.”
The Human Brain Project – Too Good to Be True?

Roughly 10 years ago, scientists announced a very ambitious project which aimed to develop supercomputers to incorporate and integrate the immense pile of neuroscience research data of multiple decades into a complete digital simulation of the brain. Approved and funded with one billion euros from the European Commission, the Human Brain Project (HBP) was supposed to gather current knowledge on how the brain functions and finally be able to extrapolate the unknown [1,2].

Vision And Ambition

The initiative was announced with great publicity and provided with an exceptionally long funding period for 10 yrs, including a 3 yrs kick-off period, followed by 7 yrs of implementation in order to conjoin electrophysiological, imaging, and neural modeling and engineering data into a realistic model of the brain’s function [3]. Despite the immense funding, from the start, notable figures from the neuroscience field (e.g. Neuroscientists Alexandre Pouget of the University of Geneva and Gilles Laurent from the MPT for Brain Research) have criticized the project as too ambitious, raising unrealistic expectations, and deemed the funding still insufficient.

Ambition vs. Reality

Since its launch, the HBP was heavily criticized and already by 2014 rendered a big mistake by e.g. Miguel Nicolelis [4]. Within only two years after its approval, the project was intensively disputed among neuroscientists, especially regarding certain management decisions which involved conflicts of interest [6] and subsequent changes in the scientific focus [5,7]. Several supporters had withdrawn their participation and even requested the European Commission to reconsider funding. Eventually, the HBP underwent significant restructuring regarding, in part, its management, including removing the visionary Henry Markram from the leading board. Such a big and complex project as the HBP should have been designed with checks and balances initially to prevent such disputes. Hence, some argue that mainly intransparencies in the decision-making process in the European Commission and the intermingling of politics and science funding allowed such unfavorable developments in the first place [8].

From Big Data to Bigger Data?

While the HPB endeavor to integrate neuroscience research data from multiple fields surely demands massive computational efforts, during this period of heavy disputes among the involved scientists, the initiative has allegedly been downgraded to a massive IT project, bearing little advances for neuroscience [4,9]. Indeed, the creation (and curation) of more data alone, does not yet bear new insights. Around 2016, upon entering its second funding phase, the focus of the HBP was significantly shifting away from experimental (basic) neuroscience towards human imaging data and descriptive data on e.g. gene expression and connectomics across brain structures. While this type of knowledge is certainly important and was largely lacking at the time, such simulations alone do not suffice to allow testing of detailed hypotheses, and thus assessment of neuronal function [9]. In order to understand brain function, it became a central goal of the HBP to develop and employ information and communication technologies to advance collaborative research, sharing tools and data to eventually allow “decoding of the human brain” [10].

Dreams Coming True?

One development arising from the HBP since then is the research infrastructure EBRAINS. It provides researchers with sophisticated tools, resources, and applications, like the “Medical Informatics Platform” allowing e.g. the analysis of sensitive patient data without those data ever leaving the hospital [11], or individual modeling of patient brains for e.g. epilepsy-related surgery [12].

In 2020, the HBP entered its final phase, focusing on neural networks and how they affect consciousness as well as artificial neural networks [2]. Although not necessarily contributing by generating data or making any functional predictions, any advances during the HBP initiative regarding the development of specific data integration platforms and neuroinformatic methods are valuable [6] and have contributed to several hundred publications [11]. In its final period, the HBP also focuses on the sustainability of the developed research infrastructure to make sure it remains available to benefit neuroscience research also in the future by integrating its developments into existing European research infrastructure, involving e.g. the European Brain Council (EBC) and the European Brain Research Area (EBRA) [11].

Starry Goals

There is this motivational quote “Aim for the moon – even if you miss you’ll land among the stars” and the HBP did for sure. The initiative did certainly not simulate a human brain as envisioned at the beginning. Whether or not the project did or will meet its goals by the end of its final funding period may be judged by the associated publication record [11,13], however, the initiative inarguably contributed to the advancement of neuroscience by furthering the development of the necessary computational infrastructure to access and process existing data.

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References:
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[5] https://www.nature.com/articles/s11131a
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[10] Amunts et al., 2016, Neuron
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Genetics plays a hugely important role in the field of neuroscience. The use of genetic tools and approaches has made it possible to study how genes underpin the function of the nervous system. The application of genetics in neuroscience has evolved rapidly in the last few decades. This has led to the discovery of a vast amount of new information about the role of genes and genetic information in the development and function of the central nervous system.

**Past: Developing Genetic Tools**

The genetic approaches used in neuroscience and other fields have changed drastically and their usage has exploded in recent times. Huntington’s disease-causing gene HTT, also called Huntingtin, was the first human disease gene to be genetically mapped. This was done in 1983 revealing the gene’s location using restriction fragment length polymorphisms (RFLPs) [1]. These were detected as differences in the sizes of restriction fragments observed in Southern blotting. The RFLPs were detected using probes which were then used in constructing a genetic linkage map to localize the disease gene [2]. This was a long, complicated, and labor-intensive process. Today, RFLP analysis is largely obsolete due to the emergence of inexpensive DNA sequencing. However, it was very important for localizing several disease genes such as HTT.

In the 1980s and 1990s genetic tools developed, quickly leading to the first knockout mouse in 1987 and the first cloning of a mammal nine years later in 1996 [1]. Eventually this led to the development of omics-approaches of the 2000s. The omics-approaches involve a comprehensive assessment of a set of molecules [3], and have become increasingly important for several fields of study including neuroscience.

Neurodevelopment is a hugely complex process that is under tight genetic control. Thus, genes implicated in development are often studied. One such example is the Ras/Rap GTPase activating protein, SynGAP. SynGAP was identified using a two-hybrid system in 1998 testing for binding between molecules [4]. The two-hybrid system is still in use to study protein-protein and protein-DNA interactions [5]. The discovery of SynGAP also shows, in part, how much technology has changed and improved in the years from mapping the HTT gene to the identification of SynGAP.

Identification of a gene of interest is only the first step. Genetic approaches in neuroscience are used much more extensively. SynGAP is a good example of this. After its identification in 1998, it was further characterized using genetic methods. This was used to show that there are several different isoforms of the gene, primarily expressed in the brain, particularly in the postsynaptic density [4]. This led to the first evidence that SynGAP regulates synaptic strength, plasticity, and long-term potentiation (LTP) [6]. In humans, SynGAP mutations were also implicated in disease [7]. This finding was in large part due to the omics-approach which has been made possible using genetic tools in later years. Since then, multiple patients have been identified with SynGAP mutations which result in a continuum of intellectual disability, epilepsy, and autism spectrum disorder (ASD) [4]. Recently, this knowledge has been expanded upon and much more information has been discovered largely due to the development of multi-omics approaches and advances in sequencing technology.

**Present: From Bench to Bedside**

In the last decade, next-generation sequencing (NGS) has contributed significantly to the field in both the research lab and clinic. One such advance is the use of targeted sequencing. Here, researchers use public datasets with known candidate genes as a starting point. This allows for the study of, for example, SynGAP variants in patients [8]. Another important advance is the emergence of whole exome sequencing (WES). Two approaches of WES are possible to either find rare inherited variants or de novo mutations. Identification of de novo variants can be done with smaller sample size and is done more frequently today [9]. One of the major advantages of WES is that it targets all coding regions of the genome without biases. Moreover, it is cheaper, quicker, and easier to analyze than whole genome sequencing. However, WES does not include non-coding regions.

**Evolution of Genetic Approaches**

<table>
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<tr>
<th>1983 Genetic Mapping of HTT</th>
<th>2001-2003 Human Genome Project</th>
<th>2011 FDA approve NGS for clinical use</th>
<th>Future The use of NGS for personalized medicine is routine in the clinic</th>
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<tr>
<td>1998 Identification of SynGAP</td>
<td>2005 Next generation sequencing (NGS)</td>
<td>2011 FDA approve NGS for clinical use</td>
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Elisa Pedersen | 2021
In the research setting, these recent sequencing technologies enable the discovery of risk genes. Next, functional genomic studies can be performed to elucidate the pathogenic mechanisms and biological pathways involved. With recent advances, this can involve patient-derived stem cell disease models, such as the CRISPR-Cas9-modified cells or 3D cortical organoids. This may lead to the development of new therapeutic strategies. An example of this is Creson et al. who wanted to explore the effects of SynGAP on cognitive impairment and seizure susceptibility. They used a SynGAP1 heterozygous mouse that reactivates the targeted allele and re-expresses SynGAP protein upon Cre activation by tamoxifen. Using this mouse model, they found that restoring an adult gene that boosts low levels of SynGAP protein can reverse deficits in remote memory, lowers seizure threshold, re-balances neural excitability, and improves hippocampal/cortical function [10].

**Future: Promising Therapeutic Implications**

NGS has led to more accessible sequencing and identification of several risk genes, such as SynGAP, which may enable healthcare professionals to create individualized care plans for patients. NGS allows for rapid sequencing of various genes simultaneously at a lower cost [6*]. This has made genetic testing accessible in the clinic and we will likely see this become more widespread in the next few years. The use of these tests has already improved the diagnosis of diseases, such as SynGAP-associated intellectual disability [8]. This is a step towards personalized medicine which is already underway as the sequencing results for a patient may affect the choice of pharmacological intervention or behavioural treatment. However, this is not currently routinely used in clinical practice. This could change in the coming years. One example where this could be used is the diagnosis of SynGAP disorder. The development of genetic technologies, such as sequencing, has contributed to the discovery of genes, enabling scientists and clinicians to link them to disorders.

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[9] Cardoso et al., Hum Genomics, 2019
[10] Creson et al., Elife, 2019

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**Glossary**

Southern Blotting: molecular biology technique used to detect a specific DNA sequence in a sample. Here the DNA is separated by electrophoresis and transferred to a membrane. Here the fragment is detected by probe hybridization [1*].

RFLP analysis: a technique that uses variations of homologous DNA, called polymorphisms, to distinguish individuals, or species or to pinpoint the locations of genes within a sequence [2*].

Two-hybrid system: a technique that is based on activation of a downstream gene by the binding of a transcription factor onto an upstream activating sequence (UAS). The transcription factor is split into two separate fragments, called the DNA-binding domain (BD) and activating domain (AD). The BD is the domain responsible for binding to the UAS and the AD is responsible for the activation of transcription. This can then be used to look for protein-protein interactions and protein-DNA interactions [3*].

Long term potentiation: main form of synaptic plasticity reflecting the activity of synaptic information storage processes, and has been identified as the prime candidate to be the cellular correlate of learning and memory [4*].

De novo mutations: A genetic mutation that is present for the first time as a result of a mutation in a germ cell or a mutation that arises in the fertilized egg itself during early embryogenesis [5*].

Next-generation sequencing (NGS): a new type of sequencing developed to allow for parallel sequencing that offers high throughput, scalability, and speed. NGS is used to determine the sequence of nucleotides in entire genomes or targeted regions of DNA or RNA [6*].
Whole exome sequencing (WES): a type of NGS that involves sequencing the protein-coding regions of the genome. The human exome represents less than 2% of the genome but contains about 85% of known disease-related variants. This makes it more cost-effective than sequencing the whole genome [7].

Organoids: are complex clusters of organ-specific cells, such as those from the stomach, liver, or bladder. Organoids are developed from stem cells/progenitor cells. Organoids self-assemble when given a scaffolding extracellular environment. This allows them to grow into microscopic and usually disorganized versions of organs. This makes them viable for 3D study [8].

Personalized medicine: this can also be called precision medicine. Using this type of medical practice medical decisions, practices, interventions, and/or products are tailored to the individual patient based on their predicted response or risk of disease. This is often based on their genetic information or similar [9].

The sweet smell of fruit doesn’t normally send mice running. But when researchers paired the orange cherry almondly scent of the chemical acetophenone with a painful electric shock, lab mice quickly learnt to fear it [1]. Along the way, extra neurons sprouted in their noses and the specific smell processing centers of the brain, making them super sensitive to the smell. While this result isn’t surprising, what is really shocking is that mice pups and their offspring were also startled by the smell of acetophenone and had the same extra neurons as their fathers, despite never being exposed to either their fathers or to the fruity scent before! But, how could the pups inherit something their fathers learned?

Well, while basic genetics teaches us that only DNA gets passed along to the upcoming generation, characteristics like memory, scars, or giant muscles can’t be transferred since acquiring them doesn’t alter the genetic code. Although responding to heterogeneous environmental stimuli is crucial to the survival of organisms, many a times it manifests itself as alterations in the structure and function of the nervous system. Thus, a factor that influences the overall development of the nervous system is the exposure of the parents to salient environmental stimuli before the conception of their offspring. Such imperative information exchange could be an effective way for the parents to inform their offspring about the importance of specific environmental features that they could potentially encounter in their future environments. Therefore, it turned out that instilling fear in the mice did in fact stimulate genetic modifications or changes, not in the DNA sequence itself, but instead in how that code was read and used in the mice’s bodies.

Epigenetic Modifications Shape Our Experiences

In every cell, the biological machinery constantly translates DNA into the proteins required to carry out vital functions of the body [2]. Specific chemical modifications of the nucleotide bases and proteins which are attached to the DNA turn gene transcription on and off, thereby telling the machinery which proteins to produce and in what quantities. These switches are known as epigenetic tags. Even though every cell in your body begins with the same DNA sequence, give or take a couple of letters here and there, the text has different patterns of expression in different cell types – a hepatocyte doesn’t need to follow the same parts of the instruction manual as that of a neuron. Interestingly, the switches in each cell aren’t set in stone! Teaching those mice to fear the fruity smell switched one of their smell-sensing genes into overdrive. Although researchers don’t know where or how exactly the switch was flipped in mice, they did analyze one cell type which seemed to be involved. That was the mice’s sperm cells. It will eventually pass on their genetic material and make the next generation of mice immensely sensitive to acetophenone [1].

Interestingly, rodents aren’t the only creatures demonstrating this type of behavior and weird type of inheritance. In the Överkalix population in northern Sweden, men who suffered extreme insulin sensitivity in response to winter famines went on to have healthy sons. This was further observed in their next generation with visible optimal health characterized by the absence of heart disease or diabetes, a concept known as transgenerational inheritance [3]. Potentially, this demonstrates that the transgenerational associations between paternal experiences and health outcomes could arise.
from cultural inheritance or social patterning. This demonstration of an exposure-sensitive period as exhibited by experiencing the famines during the mid-childhood period prior to puberty in the parents, provides a potential link for some other form of transmission which could exist between generations. Surprisingly, the upcoming generation of the Swedish men lived an increased life span of 32 years on average as compared to the grandsons of individuals who had not yet observed any condition such as the famine. The switches triggered by the Swedish famine are still being discovered; what is known, however, is that the connection between different epigenetic switches or tags in mice can be used to link these inheritance patterns in humans [3].

The emergence of molecular epigenetics

The rise of molecular epigenetics over the last few years has significantly shaped the discourse about the sociality and susceptibility to environmental modifications in the context of the brain as an entirely new, unexplored dimension [2]. In recent years, epigenetics has emerged as one of the most advanced examples of the new post-genomic and context-dependent view of contemporary biology. Considering the rapid emergence of the field, in this article, we shall delve deep into the history and development of epigenetics and its relevance to neuroscientific research.

Epigenetics deals with the study of heritable changes in gene expression or phenotype caused by mechanisms other than alterations in the DNA sequence [2]. In other words, it is the study of gene transcriptional levels, potential, and inertia. As Michael Meaney, a neuroscientist and clinical psychologist at McGill University said, “There are no genetic factors that can be studied independently of the environment, and there are no environmental factors that function independently of the genome. At no point in life is the operation of the genome independent of the context in which it functions” [2]. Therefore, it is vital to look at the environmental events occurring at the later stages of development that can alter a developmental trajectory based on the studies of nature (genes) and nurture (environment and experience).

Interestingly, a study conducted at the Allen Discovery Centre for Human Brain Evolution demonstrated the importance of understanding DNA mistakes, also known as somatic mutations [4]. Let’s consider the following scenario: during the initial period of human development if something very small went erroneous, for instance if the cells made a small mistake while copying their DNA. As the daughter cells of those mistake bearing cells continue to grow and divide, all other cells they generate contained the same DNA mistake. Therefore, the earliest periods of your development influence the fate of the rest of your body. Our bodies consist of potentially thousands and thousands of such mostly innocuous, little mistakes. These mutations arise once the body is already formed but rarely exhibit immediate effects. However, the gradual accumulation of these cell-to-cell differences over a lifetime certainly adds up! This suggests that even though small mutations may rarely have any discernible effects on your life, they do mark the cellular history which is written in our cells.

Our cellular biographies

To sketch the detailed map of our cellular histories, in the nineteenth century whilst the science of genetics and developmental biology was making rapid progress, leading biologists and embryologists were using methods, tools, and procedures that seldom took into consideration genes and gene action. It was only towards the middle of the twentieth century that the relationship between genetics and developmental biology was elucidated [2]. One individual who was knowledgeable in both fields was Conrad Waddington (1905-1975) [2]. Termed from the Greek word “Epigenesis”
the previous theory of development which stated that the early embryo is undifferentiated was subsequently changed to epigenetics. Waddington, who was the Buchanan professor of genetics at the Edinburgh University, considered epigenetics to be similar to embryology. According to him, epigenetics was defined as the unfolding of the genetic program for development [5].

The probably broadest explanation of the emerging field can be given as follows: Epigenetics is the transmission and conservation of information that is not based on the DNA sequence, such as the perpetuation of cellular phenotype via meiosis or mitosis. Interestingly, the process is not solely limited to DNA-based transmission; it is also protein-based [5]. Prion-based epigenetic inheritance represent a viable, protein based system for epigenetic memory! Briefly, prion proteins are synthesized in an inactive form however, when stimulated by an exogenous signal they convert into an active form that can potentially alter a cellular phenotype. Once activated in a cell, the prion proteins are able to viably establish a self-perpetuating biochemical reaction that is both persistent across time and is heritable across cell division [5]. Suggestive, those phenotypes which can be inherited by daughter cells are perpetuated past cell division using protein-based or prion-like mechanisms. The principle criterion, however, is heritability! Another approach posits that the phenomenon of epigenetics deals with stable maintenance of gene expression changes that consist of the physical identification of DNA or its associated proteins. This subsequently allows genotypically identical cells to become phenotypically distinct, such as a neuron that is phenotypically distinct form a hepatocyte [5]. Interestingly, a common theme amongst canonical criteria for epigenetics is the existence of a mechanism for storing and perpetuating a “memory” at the cellular level. Historically, a central tenet in the field of epigenetics has been that the epigenetic marks or traces are laid as part of the development and are immutable within each cell and subsequently inheritable across cell divisions [5]. These epigenetic molecular mechanisms have also been shown to mediate acquired experience-dependent modifications in cognition and behavior [2].

**The Case of Drosophila melanogaster**

Another leading biologist who contributed to bridging the gap between genetics and developmental biology was Ernst Hadorn (1902-1976) [5]. The majority of Hadorn’s studies characterized developmental processes in Drosophila melanogaster, which was highlighted in his book titled “Developmental Genetics and Lethal factors” [6]. Hadorn and colleagues deciphered the properties of imaginal discs of Drosophila. These discs are representative of regions of the embryonic tissue that are located within the fly larvae. Briefly, the work highlighted that each of the discs later develops into a specific adult structure: two for each of the wings and two for the antennae of the fruit fly [6]. Interestingly, each of the disc cells was undifferentiated and can be determined to differentiate only later in their development. Furthermore, the disc tissue was subsequently grown in the abdomen of adult flies, and passedage from fly to fly, across offsprings. When the disc tissue was acclimatized with the hormone ecdysone, the tissue differentiated into the appropriate adult structure [6]. In other words, Hadorn and colleagues were able to demonstrate that the determined state was heritable, sometimes even over several cell divisions.

Therefore, it is interesting to note that genes and experiences are mechanically intertwined! Epigenetic mechanisms contribute significantly to this intertwining.

**Epigenetic Tagging in the CNS**

In the broader context of neurobiology, this emerging field has deep implications for the historical debate of the role of genetics vs. environment in the regulation of behavior. Contemporary studies indicate that environment and experience act in unison by altering gene readout in the CNS and thereby affecting behavior [2]. A major part of the processes by which the environment and exposure to stimuli alter individual behavior include mechanisms such as covalent modification of the DNA via DNA methylation, a type of chromatin structure regulation via post-translational modifications [2]. Other modifications include regulation of gene-expression via non-coding RNAs, non-genic DNA or histone modifications (including acetylation, methylation, ubiquitination, SUMOylation) [2].

Previously, epigenetic mechanisms have been shown to have a vital role in nervous system development. Briefly, neurons express a complement of proteins which are essential for their function. These include proteins which have a role in neurotransmitter release, excitability regulation, and maintenance of transmembrane potential to name a few [2]. These proteins are governed by a neuron-restrictive silencer element (NRSE) within their promoters and have the ability to completely silence a gene in non-neuronal cells [7]! Upon the binding of NRSEs to transcription factors such as RE1-silencing transcription factor (REST), gene expression was shown to be repressed [7]. These observations are indicative that REST-dependent gene silencing and therefore cellular differentiation, involves the action of several proteins and transcription factors which bind to the complex, either via decrease in histone acetylation or enhancement of DNA methylation mark the DNA epigenetically for repression.
Gene-environmental Regulation of the Circadian Clock

In addition to the potential role of epigenetics in context to neurodevelopment and neurogenesis, investigation of how epigenetic mechanisms regulate vital processes in the CNS has also been elucidated in context to circadian rhythms. The physiology of humans is modulated by the time of the day. Daily rhythms persist in the absence of extrinsic environmental cues and have a period of approximately 24 hours [7]. This periodic activity is known as circadian rhythm. Governed by the master clock which resides within the suprachiasmatic nucleus (SCN), situated in the anterior hypothalamus, it entrains the body’s natural rhythm to light! Within the core of any circadian clock is the transcription-translation feedback loop, which is modulated by epigenetic mechanisms.

Although the genome likely undergoes daily modifications in the epigenetic status, the acetylation of specific histones such as H3 and H4 are differentially regulated during a circadian rhythm cycle [7]. These histones are associated with promoters of genes (such as period genes) which play a canonical role in the formation of the core molecular clock. Interestingly, it was demonstrated that the induction of specific histone deacetylases (HDAC) inhibitors such as trichostatin A into the SCN increased the expression of clock genes, indicative that epigenetic mechanisms alter the expression of molecular elements of the circadian clock [7].

Epigenetic Dysfunction: Role in Cognitive Disorders

Derangements in the molecular elements of the epigenetic machinery have recently emerged as the causal basis for human cognitive dysfunction [7]. Therefore, it is worthwhile to consider that the active utilization of these mechanisms is necessary for normal cognition and the maturation of the post-development CNS.

In case of pathology, several disorders can be attributed to the dysfunction in epigenetic tagging of the genome! Amongst the common senile forms of dementia, Alzheimer’s disease (AD) is one such neurodegenerative pathology which exhibits epigenetic dysregulation. AD occurs in part due to the increased accumulation of amyloid-beta peptides in the brain, which are formed by the endo-proteolytic cleavage of amyloid precursor protein (APP) [2]. Interestingly, the cleavage of APP results in the production of an extracellular β-amyloid fragment but also an intracellular fragment known as the APP intracellular domain (AICD). The intracellular domain of the APP acts as a notch-like transcription factor and regulates transcription of adapter proteins such as Fe65 and HAT Tip60 [7]. This suggests that pathology in AD might be caused by a dysregulation of histone acetylation. Similarly, patients suffering from the neurodevelopmental disorder Rett syndrome exhibit a loss of function (LOF) mutation in the MeCP2 gene, which is a methyl-DNA-binding protein [7]. In physiological conditions, this gene is involved in long-term memory formation and regulation of synaptic plasticity [7]. These suggest that the dysregulation of normal epigenetic machinery can have consequences on normal cognition and, furthermore, elucidate that drugs which target the epigenome can emerge as novel therapeutic targets [8].

To conclude, the field of epigenetics is rapidly growing and it is vital to note that both the environment and individual lifestyle can play a role in how the genome interacts to influence epigenetic changes. Although our epigenetic marks are more stable during the time course of adulthood, they are considered to be dynamic and modifiable by lifestyle preferences. In addition, the environment has a powerful impact on the modification of epigenetic marks and disease susceptibility. In recent years, pollution and environmental toxins have emerged as an area of focus [7]. Toxins and air pollution can potentially alter the methyl tags on DNA and thereby increase one’s risk for cognitive deficits [7]. Consumption of vitamins such as vitamin B [9], in conjunction with a healthy diet, may serve as a barrier against hazardous epigenetic effects of environmental toxins to combat the effects that toxins impose on the body.

Epigenetics therefore, is a phenomenon with wide-ranging, powerful effects on many aspects of biology, with an enormous potential in human medicine. The field has ability to fill in some pretty diverse gaps in our understanding of human health and disease, and to provide scientific mechanisms for so many of our lived experiences. So, the next time you’re wondering why identical twins aren’t well, identical or you’d like to understand something that isn’t genetic or lastly, you got a weird result from an experiment that makes little sense: all can probably be answered by Epigenetics.

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[8] https://www.whatisepigenetics.com/fundamentals
Clinical trials are defined by the Charité - Universitätsmedizin Berlin, the largest hub of clinical research in Germany, as “research studies involving human participants, which are conducted in order to test new medicines or to evaluate innovative treatments of diagnostic procedures” [1]. Modern-day clinical trials take place under strict regulations with emphasis on adequate controls and high ethical standards. However, it took long for them to evolve into their present form. In this article, we dive into the history of clinical trials and the milestones that made them into what they are today.

The First Clinical Trial
The first description of an intervention resembling a clinical trial is found in the Book of Daniel of the Old Testament [2,3,4]. The passage describes a nutritional experiment in which a group of people eating only meat and wine is compared to another group eating only pulse/vegetables and water. Even though the authenticity of the passage is debatable, it is evident that by the time the passage was written – around 150 BC – the ideas underlying clinical trials were present [3].

While other events resembling clinical trials occurred, what is generally accepted as the first recorded planned comparative clinical trial of the modern era is a study by Dr. J. Lind. In 1747, he investigated the efficacy of six dietary treatments for scurvy [3,5,6], a disease caused by vitamin C deficiency that used to kill thousands of British sailors each year [3]. His study included 12 scurvy-affected sailors, two per dietary group, and identified the citrus diet, composed of oranges and lemons, as the best treatment [6]. As famous as it may be, Lind’s study had many pitfalls that, at least in theory, are avoided by most studies in our time. For example, even though he had a concept of control, shown by the fact that his subjects were „as similar as [he] could have them” [6], he later notes that two of the worst patients had ended up in the same dietary group, which could bias the results of his study.

We can draw an interesting parallel between Lind’s study and the modern-day relationship between science and policy-making. At the time, citrus fruits were expensive, so it took 50 years before they were implemented in the British Naval diet, despite Lind’s clear findings [3,4]. Today, healthcare advancements are still heavily influenced by economic considerations and political plays, leading to delays in adopting improvements suggested by the scientific community.

Placebo
The inclusion of placebos in clinical trials revolutionized the field and helped isolate the true effectiveness of treatments. While placebos were already in use by 18th-century physicians to comfort patients in lieu of actual treatment, Flint’s study on rheumatic fever in 1863 is often identified as the first placebo intervention [4,7-10]. Flint gave 13 patients an herbal extract instead of the orthodox treatment of the time and saw no difference in the development of the disease. Based on this, he concluded that rheumatic fever receded naturally over time and that the established medication given had no actual effect. Nevertheless, it took longer for mainstream medicine to recognize the need for placebos to validate scientific findings.

Randomization
Numerous earlier studies attempted to implement randomization. In 1898, Fibiger used alternate assignments to divide diphtheria patients into groups [11]. Nowadays, this is not considered ideal due to the potential bias in patients’ admission that can result from knowing what group allocation comes next [3]. The first properly randomized clinical trial is considered to be a 1948 study of streptomycin as a treatment of tuberculosis [3,10,12], in which random sampling numbers were used to assigned patients into streptomycin or control groups. Future studies adopted randomization, which is part of every properly designed modern clinical trial.

Blinding
Blinding, or masking, began to appear at the end of the 19th century, mainly in psychological studies [8]. In a single-blinded study, patients do not know whether they are in the control or experimental groups while in a double-blinded...
study, neither the patients nor the physicians conducting the study are aware of who is in which group. Blinding started becoming more common in Germany during the early 20th century. The German tradition influenced the United States, which adopted the use of masking [8]. It must be noted, however, that the proper application of the research protocol depends on randomization, which minimizes the chances of having noticeable patterns that obscure blinding. Interestingly, but perhaps not surprisingly, blinding is not always possible. For instance, in a 2006 study of the interaction between rifampicin and atenolol blinding was not possible due to the red color in urine caused by rifampicin [10,13].

Ethics

Presently, the scientific community places a strong emphasis on the ethical aspects of both animal and human studies, including clinical trials. As with basic human rights, which are considered a given in today’s first-world countries, this was not always the case. Experiments were often performed on prisoners, slaves, or otherwise disadvantaged people with no consideration of their welfare [3].

Although the issue of informed consent in human experimentation was already acknowledged in a few 19th-century cases [14], it wasn’t until the atrocities of World War II that the need for regulation, implementation, and adherence to research ethics became a prominent public concern. The Nuremberg trials of Nazi experiments resulted in the Nuremberg code of 1947, an influential set of principles defining ethical regulations in human experimentation, which emphasized the importance of subject’s informed consent [3-5, 14,15]. The adoption of this practice slowly took place from country to country, leading to 1964, when the World Medical Assembly issued the Declaration of Helsinki. This was not legally binding, but it served as the basis for international laws concerning medical research [3,5]. Nonetheless, unethical experiments continued well into the rest of the 20th century. A relatively known recent example is the Tuskegee Syphilis Study, conducted from 1932 to 1972, which investigated the natural progression of untreated syphilis. Despite penicillin being available as a treatment much earlier, the 400 black men participating in this study remained untreated, which likely resulted in the death of numerous participants [16]. Modern-day scientists stress the importance of ethical regulations; and violations thereof are both legally prosecuted and publicly condemned.

Recent Changes

In 2019, Nature Medicine published an article called “Twenty-five ways clinical trials have changed in the last 25 years” that describes the main recent changes in clinical trial procedures [17]. For example, more studies are now originated and controlled by industry instead of academia. Molecular knowledge - in terms of disease understanding, the discovery of new therapeutic targets, and the use of biomarkers for patient selection – is becoming more and more essential. Moreover, online recruiting is implemented to solve the prevalent problem of small sample sizes, something caused by low participation and complicated inclusion criteria for patients. Recent changes are also aimed to enhance the inclusion of minorities and evaluate the effect of gender, racial and ethnic background on treatment efficacy. Additionally, authorities are calling for better training of clinical research teams in good clinical practice and more standardization of experimental procedures.

An increased amount of effort is also given to trial registration, in order to improve transparency and information availability, something that is supported by modern software. Data sharing and availability are promoted, which led to the rise of open science and meta-analysis studies. Importantly, large datasets are often collected and analyzed by artificial intelligence. In addition, more ethical regulations are established, especially when it comes to privacy policies. An interesting present debate concerns the use of sham surgeries on humans. While there are obvious ethical considerations associated with these, they were proven to be an essential control in many instances [17,18]. Lastly, a recent development in clinical trials concerns the use of wearable devices that capture data remotely and in real-time, which has the potential to revolutionize the field.

Clinical trials will continue to evolve in the future, assisted by the development of new technologies for both data acquisition and analysis. Researchers continue to look for improvements in experimental design, which will benefit scientists and patients alike. Looking into the past enables us to learn from our mistakes while entering this new era of clinical research.

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[1] bit.ly/3AkQTAi
[6] Lind, Edinburgh: Sands Murray Cochran,
[7] Cullen, Clinical lectures. Edinburgh, 1772
Think back to the last time you used medication — maybe for pain relief, some cough, or maybe for a more complex health issue. What did you think about this medicine or its roots? Chances are, end-users of drugs do not think about their origins or how they started; however, scientists have probably spent countless hours developing them. The roots of the pharmaceutical industry go back to the apothecaries that tried and tested traditional remedies since the middle age, offering a significant range of treatments based on centuries of folk knowledge.

**Arab Chemistry**

In chemistry and pharmacology, Arab people developed several types of drugs after taking over the Greek theory of treatment, primarily in the forms suggested by Hippocrates and Galen [1]. The word drug was derived from Arabic (deriaq or teriaq). Besides, Arabic numbers, fractionation, and decimal system facilitated the drug dosage communication [1,2].

Early pharmacological development was partly triggered by poison and antidote, which resulted in different types of chemically produced drugs (e.g., camphor, alkali, natron salts, concentrated herbal juices, called Roob, syrups, essences, aldehydes, and alcohols as solvents) [3]. Such discoveries in pharmacology have spread in the western world and affected it greatly.

In the modern western world, perhaps the earliest written record of medical therapeutics is contained in the famous Ebers papyrus. This papyrus is originally an Egyptian 110-page medical scroll papyrus of herbal remedies and knowledge dating to around 1550 BC. One of the oldest and most important therapeutic papyri of ancient Egypt was purchased at Luxor in 1873–74 by the German Egyptologist Georg Ebers. He published the Ebers papyrus as a facsimile with an introduction and English-Latin vocabulary. It is currently preserved at the library of the University of Leipzig in Germany [1,4].

Nevertheless, the pharmacological industry as we understand it today has its beginnings in the second half of the 19th century. While the scientific role of the 17th century had expanded the views of experimentation and rationalism, the industrial revolution changed and sped the production of goods in the late 18th century. But combining the two concepts for human health benefits was a relatively late development.

**Germany’s Pharmacology**

At that time (18th century), pharmaceuticals were usually based on alkaloids which are naturally occurring compounds containing carbon, hydrogen, nitrogen, and usually oxygen, and are primarily found in plants. Alkaloids possess a variety of pharmacological potentials in modern medicine because their effects include, for example, analgesic (e.g. morphine), antinecancer (e.g. berberine), and antibacterial (e.g. ciprofloxacin) [5,6].

The German firm E. Merck who started in Darmstadt in 1668, was the first to produce alkaloid pharmaceuticals on an industrial scale. A second-generation member of the Merck family discovered papaverine, an important alkaloid for its role as a vasodilator agent and an antispasmodic drug [7]. Later, the Merck family continued their research and discoveries in the pharmacological field. Now it is known as the Merck group, having around 250 companies working in three business lines; healthcare, life sciences and performance materials [8]. After Merck’s, other large German producers entered the market between 1885 and 1888, such as BASF, Kalle & Co., and Bayer [9].

**America’s Pharmacology**

Pfizer was founded in 1849 by two German immigrants in the USA, initially as a fine chemicals business. Their business expanded rapidly as demand for painkillers and US penicillin to treat soldiers during the American civil war was high, and by 1944, Pfizer had become the world’s largest producer of penicillin [10]. Another young man who decided to enter the pharmacology world because of the war is the naval doctor Edward Robinson Squibb, who served in the Mexican-American war. The war pushed him to develop different types of drugs, such as portable medical kits containing morphine, surgical anesthetics, and quinine to treat malaria [11,12].

**The Time Between The Two World Wars**

What marks this time is the invention of insulin and penicillin. Between 1918 and 1939, Frederick Banting and Charles Herbert Best collaborated with the scientists at Eli Lilly to isolate insulin that could treat diabetes, which up until that point was a fatal condition. Later on, they were able to purify the extract sufficiently and industrially produce and distribute it as an effective medicine [13]. However, the breakthrough invention that almost has no parallel discovery was penicillin, “the miracle drug.” On the third of September 1928, Fleming...
returned to his laboratory after spending a holiday with his family at Suffolk. Importantly, before the holiday, Fleming inoculated staphylococci on laboratory culture plates and left them on a corner in his laboratory. After Fleming returns, he noticed that one culture was contaminated with a fungus and that the colonies of staphylococci that surrounded the fungus directly had been destroyed. In contrast, other staphylococci colonies which were a little distant from the fungus were normal. Fleming grew the mold in pure culture and found that the culture broth contained an antibacterial substance [14, 15]. After several months of calling the substance that destroyed the bacteria “mold juice” or “the inhibitor,” on the seventh of March 1929, Fleming finally named the antibacterial substance penicillin, after the mold it stems from *Penicillium notatum*” [16]. After this great discovery, an international collaboration including Merck, Pfizer, and Squibb worked on mass-producing the penicillin drug during World War Two, saving thousands of soldiers’ lives [12].

**After The War**

The appearance of social healthcare systems like the UK’s National Health Service (NHS) in Europe created a more structured system, both for prescription of drugs and their payments. NHS brought in a price-fixing scheme in 1957. This scheme allowed a reasonable return on investment for drug manufacturers, setting the motivation to invest in new medicines [12].

NHS was founded on the fifth of July 1948 in England and Wales. In order to care for hospitals patients, an approximated 125,000 nurses and 5,000 consultants were available. The principles of the NHS were to provide a comprehensive service funded by taxation, available to all and accessible at times of need [17]. The NHS was based on recommendations of the British economist and politician William Beveridge, who was a progressive and social reformer. According to Beveridge, a nationalized health service was just one way Britain could help beat want, disease, ignorance, squalor, and idleness [18].

Meanwhile, in the US, the pharmaceutical industry was booming as part of the world’s biggest and most dynamic economy. The US pharmaceutical growth was helped by generous funding from the government, with the National Institutes of Health (NIH) seeing its federal funding rise to nearly $100 million by 1956. This investment fuelled the development of drugs in the coming decades [12].

NIH was initially founded in 1930 as a laboratory within the Marine Hospital Service to investigate diseases such as cancer and finds new treatments. NIH foundation marked the beginning of the partnership of several universities in the US for health and diseases research. One of the crucial decisions by the NIH that in the 1960s, it has required the approval of all grantee institutions for any research proposals, including human experimentation with review boards. NIH does considerable research for heart disease, cancer, strokes, and DNA [19, 20].

**Social Impact of The Drug Industry**

Clearly, these drugs and many others speak for themselves. Many other scientists and drugs that could not be mentioned in this report because of the limited space have changed the world and saved millions of lives. The benefits of the drugs cover almost all aspects of human biology and even social life, such as the contraceptive pill. Introduced in 1950, it impacted society by allowing women to effectively control their fertility and enabled sexual equality for the first time [21].

However, as the pharmacology industry grew wealthy, the potential ethical conflicts of making money from selling healthcare products became increasingly apparent. An example of this ethical conflict is the research into new antibiotics, which have declined as they do not create the revenues big pharma is looking for – and this occurs when the world is still coming to grasp the scale of antimicrobial resistance threat [22].

George Merck himself addressed such ethical conflict declaring that “We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we remember it, the larger they have been.” [23].

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Nathan:  
There’s a qualification to you being impressed?

Caleb:  
No! No qualification to her. It’s just in the Turing test… the machine should be hidden from the examiner.

Nathan:  
No, no, no - we’re way past that. If I hid Ava from you, so you just heard her voice, she would pass for human. The real test is to show you she is a robot, and then see if you still feel she has consciousness.

In this excerpt from the film Ex Machina (2014), the AI designer Nathan proposes an update to the famous Turing test [1], having introduced his programming employee Caleb to “Ava”, Nathan’s latest AI humanoid. Instead of measuring an artificial system’s intelligence by judging whether it passes for a human interlocutor, Nathan suggests a different benchmark for what it means to be human-like. For him, the key question is: Can an AI system be – or trick us to believe it is – a conscious creature?

Studying Consciousness Versus Creating It: What Can Machine Consciousness Research Learn From The Neurosciences?

Just because it stems from a science-fiction movie doesn’t mean the idea is implausible or even futuristic. In fact, the possibility of machine consciousness has existed in the background since the field’s very beginning, with the 60’s cybernetics. However, it was only explicitly addressed in the 2001 Symposium “Can a Machine Be Conscious?” in New York. In this interdisciplinary meeting, philosophers, neuro- and computer scientists agreed that “there is no known law of nature that forbids the existence of subjective feelings in artifacts designed or evolved by humans” [2]. In other words, the possibility that the robot “Ava” could be conscious is not mere science fiction.

Part of the motivation behind the pursuit of machine consciousness is precisely to break new ground for the understanding of our own (human) mental life, assuming this understanding is within reach. Explaining human consciousness is actually a task for the neurosciences - which have seen some but not huge advances in this particular area. For example, by formulating different models of consciousness [3], like the Global Workspace or the Integration Information, as well as by identifying various structures, e.g. the frontoparietal network or V4, as plausible candidates for its neural correlates. These discoveries have largely been made through studies contrasting neuroimages with behavioural or subjective measurements.

In contrast, the main advantage of exploring artificial consciousness over studying it in humans resides in the ‘design’ aspect. AI design provides the chance to directly intervene in the development of the mechanism supporting consciousness – an unavailable approach when dealing with human subjects, which come equipped with consciousness already. Generally, only “natural” intervention (brain injury) or indirect, non-invasive methods, like TMS or ultrasound, are available for the manipulation of human brain mechanisms, and hence for use as control cases in neuroscientific studies, allowing us to learn about consciousness through its disruptions [4].

These and other methodological limitations [5] keep hampering the progress of consciousness research. So much that, despite the fact that the discipline is still in its infancy, psychologist Steven Pinker [6] and philosopher Colin McGinn share the pessimistic view that the nature of consciousness might forever remain puzzling [7]. Machine consciousness research also inherits some of these problems, which, together with the lack of a consensus on a scientific concept of consciousness, makes the newly broken ground rather muddy. Those striving for artificial consciousness might look at the current debates on consciousness and wonder: “so, what exactly are we trying to design?” Different taxonomies of consciousness have emerged, distinguishing various aspects, kinds, dimensions, and...
levels of consciousness. Establishing which of these may apply for the case of machine consciousness could make the task of designing artificial consciousness a little more feasible, by narrowing down the necessary conditions for a creature to be conscious. It might not be the same to endow a machine with the capacity to "feel something" (as in having minimal subjectivity or sentience, which is also attributed to some non-human animals) than to make it able to be conscious of itself and its thoughts as being its own (which is taken to be exclusively found in humans). Both concepts are currently understood under the term 'consciousness', depending on the scholar one refers to. At the same time, AI designers might also decide to stay away from these debates and pave their own way, perhaps coming up with a non-anthropocentric/non-biological account of consciousness; although this would raise the question of what such model might still teach us about human and animal consciousness, if anything. In any case, it seems that the project of creating consciousness from scratch may entail greater opportunities for exploration and trial-error than merely extrospecting [8] the existing, flesh-and-blood version of it, and this makes the enterprise worth pursuing.

**Three Main Challenges for Conscious AI: The Model, The Method, and the Moral**

And yet, new challenges further complicate the picture. Specifically, three crucial questions will require substantial efforts to be fully addressed. First, if machine consciousness research chooses to catch a potentially deceiving machine? Not only do response biases take on a whole different dimension in the case of AI, behavioural proxies of consciousness in biological systems might not necessarily shed light onto artificial ones. It is anyway an ongoing project to determine which biological functions necessarily require consciousness and which ones are only facilitated by it [10]. The point is, since machines also have different cognitive capacities from humans and other animals, they might be able to perform activities that for us are only possible when conscious without requiring this capacity themselves. A known example is playing chess: Deep Blue, IBM’s computer which won against chess champion Kasparov [11], is probably not conscious - even if it plays chess extraordinarily, that is about what it can do. A different case is that of Replika, a 2017-launched chatbot that behaves like your friend or lover - a bit like a bodiless "Ava". The question “Is Replika sentient?” is among the FAQ on its website, which suggests its users do wonder often enough [12]. Both Deep Blue, based on the GOFAI (symbolic) approach to AI, as well as Replika, which works through the GPT-3 learning algorithm, are widely different examples of artificial intelligence. Since exhibiting intelligent behaviour is one of the few ways to measure a creature’s consciousness, understanding the relationship between intelligence and consciousness is a central milestone to conscious AI research.

Finally, we need to consider the possible consequences of actually ending up with a conscious AI, both for us humans and for the AI themselves. Foreseeably, being conscious would impact the functionality and performance of a robot; in an extreme case, a conscious self-driving car might decide to intentionally throw itself (and its helpless passengers) off a bridge, if it decided its existence is miserable - a more than the deficient performance of its task. Moreover, we should probably reflect on whether using conscious AI for our own purposes as a form of exploitation and might thus need to take the AI’s wellbeing into consideration, just like we do with our pets. Furthermore, just like “Ava”, conscious AI might be prone to exhibit emotions, feel pain and pleasure, and be (a)social. Conscious AI could easily act in morally relevant ways, which means someone should be held responsible for their potentially harmful actions: be it their designer, their user, or maybe the AIs themselves.

Nathan, Ex Machina’s villain, was spot on. The mere possibility of creating an artificially conscious creature calls for a new, post-Turing test: a method that enables us, knowing we are dealing with a machine, to judge whether it is conscious - so we may treat it accordingly (and not lower our guard).

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[1] Turing, Mind, 1950
[12] https://tinyurl.com/9a5wuxuz
“Science is a human endeavor. And that means that it contains and is subject to all of our brilliance and all of our bias.” - Raychelle Burks [1].

A Poignant Look at Discrimination And Individual Responsibility in Science

This solidly-made documentary Picture a Scientist made its debut on 15 April 2020 at the Tribeca Film Festival. Directed and produced by Emmy-nominated Sharon Shattuck and Ian Cheney, this film asks us to reevaluate the way we think about discrimination in science. With moving imagery and both informative and emotional interviews, the film paints the quiet dignity with which three scientists carry on.

Three Scientists, a Global Story

Picture a Scientist takes a look back at the careers of three women: Nancy Hopkins, a molecular biologist and professor of biology at Massachusetts Institute of Technology; Raychelle Burks, a professor of analytical chemistry at St. Edward’s University and successful science communicator; and Jane Willenbring, a geomorphologist and professor of geology at the Scripps Institution of Oceanography and director of the Scripps Cosmogenic Isotope Laboratory.

Interspersed between the women’s stories are interviews with experts on gender discrimination who give us a closer look at the inner workings of harassment, data-driven solutions, and implicit (and explicit) bias. Interviews with Dr. Corinne Moss-Racusin, the scientist behind the famous John/Jennifer resume study (in which a resume from “Jennifer” is rated lower in every aspect than an identical resume from John’) [2] demonstrates deep systemic issues. Dr. Mahzarin Banaji, professor of psychology at Harvard and implicit bias researcher [3], asks the audience to join her in taking the Implicit Association Test (IAT). Your results will probably surprise you.

Using the well-worn imagery of an iceberg, in which the most dangerous lurks unseen, the film delves beneath the surface to investigate how these individual experiences reflect the larger structural biases. Using data, it demonstrates not only the magnitude, but also the insidious “nature of the beast”. Most importantly, it uncovers the way in which gender discrimination undermines science itself in the end.

On The Backs of Heroes

Watching the film, I hope you will also be shocked by the rawness of these women’s stories ranging from repetitive slights – such as being mistaken for a janitor and overlooked – to gross misconduct – such as blatant sexual harassment and even, in the worst case, being driven out of science. Imagery of molecular biology labs and the Antarctic ice makes the stories come to life on the screen. With the ocean crashing in our ears, we as an audience empathize with these women, we admire their courage, but most of all, we recognize how much energy they have put into their struggles for equality. Nancy Hopkins reflects on her journey, which started with a dearth of lab space and ended in a demand for systemic change at MIT. “Such a waste of time and energy,” Nancy Hopkins admits, frustrated, “when all you wanted to do was be a scientist”.

The directors fuel this empathetic momentum with both professional and personal glimpses into the lives of these women. Between scenes, important points are reiterated in infographics designed to hearken back to a day of exclusively male textbooks, leaving the audience wondering “when was the last time I’ve really seen women in a science textbook?”.

One of the major themes of the movie is the importance of visual representation, particularly in the media. The strong representation in this film stands as a striking contrast to typical representation in books, magazines, and even documentaries. Here, Shattuck and Cheney do justice in their numerous clips of women in the field, in the lab, on the conference stage, and also as people, who live, breathe, and love science.

Calling All Scientists

At the end of the film, we as an audience are forced to reconsider our own implicit biases. Dr. Banaji’s IAT has forced us to recognize our own lack of impartiality. Dr. Willenbring’s reflection on her lack of action prompts us examine the work we are doing not only for ourselves, but for our colleagues and indeed for science itself. This is not just a film for women or even a film for women in STEM. This is a film for all scientists. As Dr. Banaji asks, “How many great discoveries have just been lost to us because we didn’t have the eyes to see?”

Picture a Scientist is available to stream on Netflix, except in Germany, Austria, and Switzerland, where it is distributed by MindJazz pictures at https://tinyurl.com/mindjazz-pas. Alternatively, institutions can request to host a screening through the website www.pictureascientist.com, just as the Berlin Institute of Health hosted a screening for International Day of Women and Girls in STEM [4]. And after you watch Picture a Scientist, you may also be interested in Shattuck’s upcoming film about a group of Dartmouth scientists who demand accountability for rampant gender discrimination there.

[1]  Picture a Scientist. Directed by Sharon Shattuck & Ian Cheney, 15 April 2020
[3]  https://tinyurl.com/72e4v4lv

Leandre Ravatt, ECN fast-track, M.Sc. MedNeuro
As we’re all scientists, we are very familiar with the systematic study of the world through observation and experiments. When talking to non-scientific folks, given that you have some decent science communication skills, people occasionally awe, for example when they see multi-colored microscopy images. And it’s true: Science is an art! But, what is art after all? The Oxford English dictionary describes “Art” as the “application of human creative skill and imagination […] works to be appreciated primarily for their beauty” [1]. In the past, we had dedicated a whole CNS issue to the concept of beauty and what is happening in our brains, and how science gets a hand on that [2]. Thus, beauty and art can be a scientific subject, but science itself is art, too!

This does not only involve illustrations of research results as a means of science communication (see also our interview with science illustrator Radnika Patnala [3]). Social media, especially Twitter and Instagram have made it easy to find exceptional pieces of art, that feature scientific content or science history, like the scientist portraits created by Kelly Stanford (@TheLabArtist). The hashtag #SciArt is a gold mine when you are as aesthetic as you are nerdy!

Often you will find that artists are scientists themselves, thus featuring aspects of their scientific work through their art. Some impressive examples are featured here on these pages.

David S Goodsell (@dsgoodsell) is a molecular biologist, artist, and professor of computational biology and creates watercolor paintings, which illustrate molecular structures of cells. His amazing paintings are available at RCSB PDB-101 [4] and also have made the cover of multiple issues of Nature journals [5,6].

Thanks to social media, a much broader (especially non-scientific) audience can appreciate the beauty and artistry in science, as pieces occasionally go viral. One such initiative that repeatedly receives attention is the annual agar art contest hosted by the American Society for Microbiology. From all over the world
Art can be Scientific

people create beautiful pieces of art by carefully placing colorful and/or fluorescent microbes on agar plates [7]. One of the many super talented participants being microbiology Ph.D. student Sarah Adkins-Jablonsky (@admiraladkins), who can also tell you exactly which strain of bacteria you’ll need.

But then again, although the hashtag #SciArt is new, science art itself is not when you consider the beautiful animal drawings of Ernst Haeckel or histologist Santiago Ramón y Cajal, which were even collected and put into a hardback book “The Beautiful Brain” (which you can also occasionally win as a prize for writing for the CNS).

The beauty of the brain and the intricate complexity of neurons have also inspired Hannah Warming (@NeedlesAndNeurons), a neuroscience Ph.D. student, to apply her artistry in a quite unexpected field: she is creating beautiful embroideries of neuroscience and biological motives (just like the famous Cajal illustration) and supports the Alzheimer’s Research UK with her proceeds.

Follow the hashtags #SciArt and #SciComm on your preferred social media platform – it’s definitely worth it! And then be inspired and get crafty yourself, as it’s a good way to balance out research stress!

Bettina Schmerl, Ph.D. student, AG Shoichet, MedNeuro

[1]  https://www.lexico.com/definition/art
[6]  https://www.nature.com/nsmb/volumes/28/issues/5
What Have We Learned, Dr. Brown?

#12 Software

Academia is becoming increasingly aware of the fact that only a minority of doctoral candidates will succeed in pursuing an academic career. The rest of us, therefore, need to face the question of what else to do with our lives and how to make a living out of it. This series aims to direct your attention to all the useful skills you have, seemingly trivial, that were acquired as prerequisites to perform your research, but which are incredibly precious outside the lab!

Today’s topic seems relatively obvious and unexciting, but it’s an important aspect nonetheless. Nowadays, nobody can imagine life without the daily use of computers. However, for most people, this merely means browsing some websites, sending emails, writing an occasional letter, and maybe run an online calendar. The average life of a graduate student involves all this, but much more intense – plus an (acquired) love-hate relationship with Excel and PowerPoint, in addition to some very specific software tools to work with data e.g. electrophysiological recordings, bioinformatics tools for in-silico cloning, microscopy imaging software, and image analysis tools... Then to process these data we use (bio-)statistics tools and eventually prepare a publication with illustrating software, create posters in layout-software, let alone writing theses and managing bibliographies.

You may ask what’s the use of knowing how to use a specific bioinformatics software when I leave the lab and academia? The main point here is not that you know how to use it, but the fact that you taught yourself! You managed to navigate through help menus, forums (e.g. Stackoverflow), and tutorials to be able to do what you want to achieve (or find out whether or not that’s possible at all) – and got to work with multiple very dissimilar and confusing user interfaces. You might even have acquired some programming skills, which – even if you will never again write a line of code in your life – will help you understand future applications and software you will encounter. You are simply not afraid of computers or software. You will be much less frustrated, as you will navigate new applications with more ease than someone who has not encountered such a ridiculous multitude of software. In your CV it may read as “competent use of software XYZ” but again, the emphasis here is not on XYZ, but on the competence.

Let us know which abilities you learned during your Ph.D. that prepare(d) you for a non-academic job if you are a Ph.D. alumni and/or recently reflected on yourself: cns-newsletter@charite.de

Your Dr Brown Team
**Our New Master’s Students 2021**

We now have nine MedNeuros (100% women), ten integrated M.Sc./Ph.D. Fellows from the Einstein Center for Neurosciences Berlin (90% women) as well as three 1st-year Neurasmus students (33% women). Additionally, we will have five 2nd-year Neurasmus students (80% women).

Of 104 applications to our Master’s program, just 30 were invited to their two interviews, focusing on both scientific and educational merits. Of the final 30 candidates, 12 declined our offer to the interviews. The remaining 18 candidates had been thoroughly evaluated, and the first 12 candidates got an offer. However, three declined for various reasons, including offers from other German institutions, scholarships or tuition-free opportunities.

For enthusiasts of statistics, the overall intake rate is: 82% female and 75% international students, emphasizing that our program is international.

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**Welcome to our Ph.D. Family**

A very warm welcome to our 14 new Ph.D. students: Lukas Faiß (Prof. Dr. Dietmar Schmitz), Marie-Louise Herzog (Prof. Dr. Karen Gertz), Dejana Mitrovic (Dr. Silvia Viana da Silva), Edyta Motta (Prof. Dr. Seija Lehnhardt), Simón Oxenford (Dr. Andreas Horn), Rina Patel (Dr. Silvia Viana da Silva), Victor Giménez Esbrí (PD Dr. Dietmar Basta), Eugenio Graceffo (Prof. Dr. Markus Schülke), Varvara Mathiopoulou (Prof. Dr. Andrea Kühn), Hugo McGurran (Prof. Dr. Seija Lehnhardt), Salabidee Mohapatra (Dr. Susanne Wegmann), Clemens Neudorfer (Dr. Andreas Horn), Nanditha Rajamani (Dr. Andreas Horn) and Selina Yogeshwar (Prof. Dr. Carsten Finke).

Selina, Eugenio and Hugo are ECN Ph.D. Fellows.
11th Neurasmus Annual Meeting

Our Neurasmus Annual meeting (July 12-15, 2021) went into round #11 with a hybrid approach. In-person events were hosted in Amsterdam, Bordeaux, and Berlin, and most of the events were available via video calls to all participants. In Berlin, students and alumni met in person and most of the events were streamed to reach our partners in Amsterdam, Bordeaux, Coïmbra, Göttingen and Laval. Some students and alumni from Göttingen and Amsterdam were able to join us here in Berlin for our event, where students presented their thesis projects and were graded according to the 2017 MedNeuro regulations.

Among having great scientific talks, the Pizza Movie Night and a Catamaran tour were the highlights of this year’s meeting in Berlin, as was the gather.town social science meeting. But clearly, the finale was the graduation ceremony with a vegetarian Israeli/Palestine dinner.

An annual meeting in person will take place in 2022 in Coïmbra or Amsterdam when we will finally be able to celebrate the 10th anniversary of the Neurasmus Program after a delay of two years!

New MSc Regulations

On December 2nd, 2020 – postponed from March to December – our Master’s program was officially evaluated by external reviewers with several discussion rounds: management (administrative and scientific personnel), heads of the modules together with the office, current and former students as well as lecturers.

We are currently filing an updated version of our regulation of the Master’s program, according to the recommendations of this panel.

Master’s Thesis Defense and Graduation

As of July 2021, we are currently planning to have the Master’s thesis’ defenses as we did before 2019: In person. Since we don’t know what the future brings, it might still take place online, but we remain hopeful that we will have an actual ceremony this year!

Humboldt Forum: MitWissenschaft – Was steckt im Kopf?

On June 17, 2021, NeuroCure researchers & ECN PIs were guests at the Humboldt Forum to talk with moderator Volker Wieprecht about neurological and psychiatric diseases such as Alzheimer’s or depression. Charité Researchers like Isabel Dziobek, Christian Rosenmund, and Craig Garner answered questions on the topic in a lively manner: How do such clinical pictures occur, what are the disease mechanisms and how to develop new therapies? As an opener, Medical Neurosciences Ph.D. student Christian Ebner presented his acrylic sculpture ‘States’, which was designed to illustrate different patterns of neuronal activity.

Missed the event? No problem at all, you may still watch the talks and find out what is in the head and why neurons fire (only in German): https://bit.ly/3xrIwY8.

Ralf Ansorg
Medical Neurosciences Office
August
31. | Workshop for early-career researchers: “How to review in interdisciplinary research” @ Science of Intelligence Cluster
25. | Prof Messoud Ashina on Deciphering the pathogenesis of migraine with human models - University of Copenhagen, Denmark: - 4:00 pm CEST

September
01. | Ben Van Calster on The enemies of reliable risk prediction - Berlin Epidemiological Methods Colloquium 2021 BEMC Talks
02. – 03. | CTNR Summer School
04. – 12. | Mediterranean Seminar for Consciousness
16. | SCIoI: Science of Intelligence Open Day

October
06. | Tracey Weissgerber: Taking shortcuts: great for travel, dangerous for writing reproducible methods sections - Berlin, Germany

November
03. | Sebastián Martinez, Glasgow, UK Causal inference in the presence of interference: generalized propensity score application on public health
10. – 12. | Accessing Mental States: The mind from different perspectives - an interdisciplinary workshop Berlin School of Mind and Brain
28. | Growing up in Science - Berlin with Prof. Dr. Christoph Harms 5:00 - 6:30 pm CEST
Schutz? Impfung!

Mit der Techniker gesunden Urlaub machen

Wir übernehmen bei privaten Auslandsreisen die Kosten für alle empfohlenen Impfungen sowie für eine Malaria prophylaxe, gegebenenfalls abzüglich der gesetzlichen Zuzahlung.

Ich berate Sie gern:
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