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# NEUROFORUM

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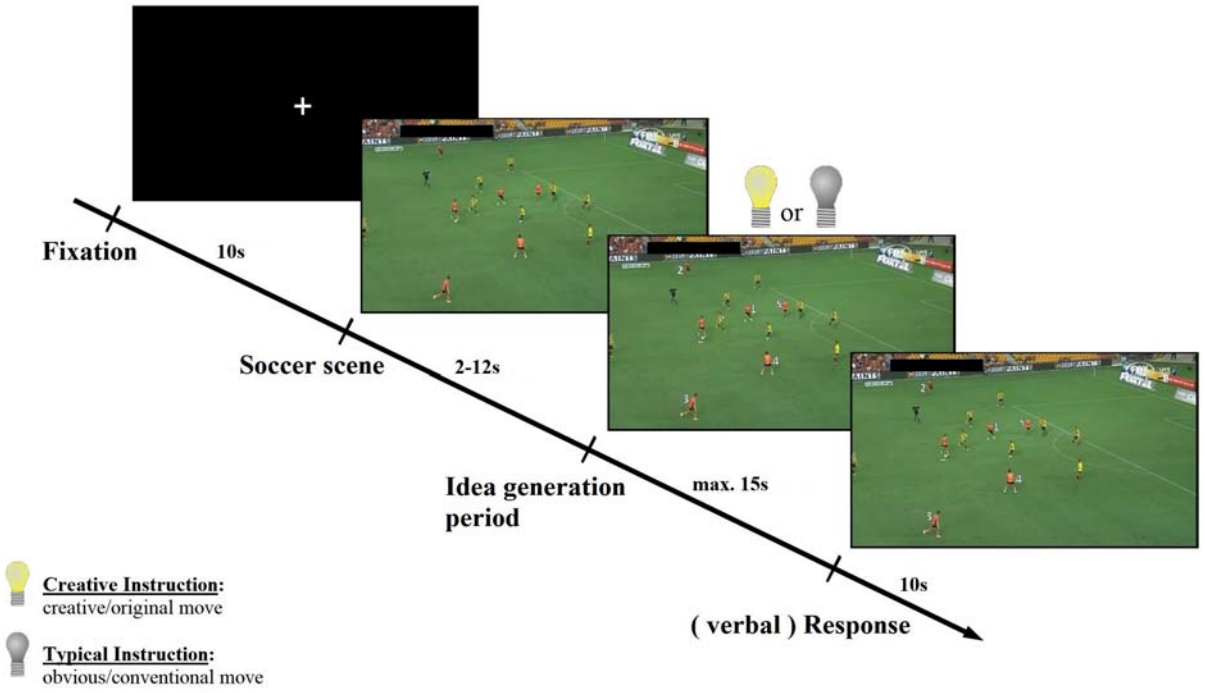


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**HERAUSGEBER** Neurowissenschaftliche Gesellschaft e.V. (NWG), Kontakt: Meino Alexandra Gibson, Max-Delbrück-Centrum für Molekulare Medizin, Robert-Rössle-Straße 10, 13092 Berlin, Tel.: +49 (0)30 9406 3336, gibson@mdc-berlin.de, www.nwg-info.de

**CHEFREDAKTEURIN** Petra Wahle, AG Entwicklungsneurobiologie, Fakultät für Biologie & Biotechnologie, Ruhr-Universität, ND 6/72, 44780 Bochum, wahle@neurobiologie.ruhr-uni-bochum.de

**REDAKTION** Susanne Hannig, Max-Delbrück-Centrum für Molekulare Medizin, Robert-Rössle-Str. 10, 13092 Berlin (Germany), Tel.: +49 (0)30 9406 3336, susanne.hannig@mdc-berlin.de

**JOURNAL MANAGER** Torsten Krüger, De Gruyter, Genthiner Straße 13, 10785 Berlin, Germany. Tel.: +49 (0)30 260 05-173, Fax: +49 (0)30 260 05-250, E-Mail: Neuroforum.Editorial@degruyter.com

**ANZEIGENVERANTWORTLICHE** top-ad Bernd Beutel, Schlossergäßchen 10, 69469 Weinheim, Tel.: +49 (0)6201 290 92-0, Fax +49 (0)6201 290 92-20 20, disposition@top-ad-online.de



**COVER ILLUSTRATION** Schematic time course of a trial of the soccer decision-making task during EEG and fMRI assessment (taken from Fink et al., 2018; https://doi.org/10.1016/j.neuropsychologia.2018.04.025). A trial started with presentation of a fixation cross for 10 s (assessment of brain activity during a pre-stimulus baseline). Afterwards brief video clips of naturalistic soccer decision-making situations are shown (ranging from 2 to 12 s). During the idea generation period, a fixed image of the soccer scene remains visible on the screen, signalling participants to imagine themselves as the acting player, and, depending on the respective task instruction, to think either of an obvious/conventional (switched off bulb, control condition) or a creative/original move (bulb switched on) while maintaining the target orientation (i.e., scoring a goal) in mind. When a participant thought of a solution/move they were instructed to press the IDEA button, and to vocalize the imagined move (max 10 s; e.g. pass to 1, then pass to 3, etc.). Oral responses were recorded via microphone and transcribed for further analyses. Cover figure provided by Andreas Fink and Mathias Benedek (https://doi.org/10.1515/nf-2019-0006, in this issue).

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# Inhalt

## Review Article



## Presentation of Scientific Institutions



## Rezension



## Nachrichten der Gesellschaft

**Review Article**

Andreas Fink* and Mathias Benedek

# The Neuroscience of Creativity

https://doi.org/10.1515/nf-2019-0006

**Abstract:** While earlier neuroscience studies on creativity have been criticized due to their heterogeneity of findings, recent studies in this field have converged to some common practices and methodological approaches, which have greatly contributed to enhance both the reliability and reproducibility of findings in this field. Relevant neuroscience findings suggest that creative cognition requires a conglomerate of neurocognitive processes involving executive functions, memory processes, internally-focused attention, or spontaneous modes of thought. Studies investigating creativity in more naturalistic, real-life settings reveal some overlap with conventional creative ideation, but also indicate that creativity and its underlying neural mechanisms are specific to the particular domain. Another trend in the neuroscience of creativity is concerned with approaches to enhance creativity, involving a broad diversity of interventions ranging from cognitively-oriented techniques to interventions using physical activity.

**Keywords:** EEG; fMRI; functional connectivity; creative cognition; divergent thinking

**Zusammenfassung:** Frühere Studien im Bereich der neurowissenschaftlichen Kreativitätsforschung wurden oft wegen ihrer heterogenen Befunde kritisiert. In der Zwischenzeit haben sich aber einheitlichere Vorgangsweisen in der methodisch-praktischen Durchführung der Studien etabliert, die zur besseren Replizierbarkeit der Befunde beigetragen haben. Einschlägigen Befunden zufolge lässt sich kreatives Denken als Konglomerat von exekutiven Funktionen, Gedächtnisfunktionen, Aufmerksamkeitsprozessen und spontanen Denkprozessen charakterisieren. Studien in alltagsnäheren Kreativitätsdomänen legen einige Überlappungen mit konventionellen kreativen Denkmustern nahe, weisen allerdings auch darauf hin, dass Kreativität und ihre neuronalen Grundlagen spezifisch für die Domäne sind. Neuere Trends in diesem Forschungsbereich beschäftigen sich auch mit Möglichkeiten zur Förderung der Kreativität, wobei hier ein breites Spektrum von kognitiv-orientierten Techniken bis hin zu Sportinterventionen zum Einsatz kommt.

**Schlüsselwörter:** EEG; fMRI; Funktionelle Konnektivität; Kreative Kognition; Divergentes Denken

Creativity is commonly defined as the ability to produce work that is novel, original and useful within a certain socio-cultural context (Diedrich et al., 2015; Runco & Jaeger, 2012; Stein, 1953). It is the engine of any progress in culture, science and education, likewise in the economical or industrial domain. From a more personal perspective, creativity has been considered as a sign of mental health and emotional well-being (Simonton, 2000), and might even have the promising potential to heal suffering (Forgeard, 2019). It is hence not surprising that creativity is increasingly attracting attention also in scientific investigations, involving a broad range of different disciplines such as economics, engineering, psychology and most recently, the field of neurosciences. In the last decade, more than 850 studies dealing with *creativity* and the *brain* were published (source: Clarivate Analytics © Web of Science), thereby tripling the number of neuroscience studies on creativity published relative to the century before. Along with the rapidly growing availability of modern brain imaging methods, this vivid research interest may be primarily attributed to continuous advancements in psychometric assessment of the different facets of creativity (Barbot, 2018; Benedek et al., 2013; Reiter-Palmon et al., 2019; Vartanian et al., 2019). Progress in the psychometric/behavioral creativity research tradition has, in turn, stimulated the development of ever more sophisticated experimental tasks and paradigms for assessing the manifold ways of how the brain works while engaged in performance of creativity-related tasks (Benedek et al., 2019).

Creativity is a multifaceted construct involving manifold processes and conditions (Simonton, 2000). A prominent example for this notion is Amabile's (1983; see also Amabile, 2013) componential theory of creativity.

***Corresponding author: Andreas Fink**, University of Graz, Institute of Psychology, Universitätsplatz 2/III; A-8010 Graz, Austria, e-mail: andreas.fink@uni-graz.at
**Mathias Benedek**, University of Graz, Institute of Psychology, Universitätsplatz 2/III, A-8010 Graz, Austria, e-mail: mathias.benedek@uni-graz.at

In this theory, creativity is conceptualized as a function of domain-relevant skills, creativity-relevant processes, task motivation, and social-environmental variables. Domain-relevant skills include expertise, factual knowledge, technical skills, and talent in the respective creativity domain. Creativity-relevant processes involve cognitive styles and personality characteristics that support novel ways of thinking. Task motivation involves intrinsic motivation, i. e. the motivation to engage in a task or to work, since it is interesting and personally challenging. And finally, creativity also depends on factors or conditions of the (social) environment that can either block or stimulate creativity (e. g., excessive time pressure, or sense of positive challenge in the work; Amabile, 2013). Neuroscience studies on creativity are particularly concerned with investigating the cognitive processes implicated in creativity, commonly referred to as creative cognition (Ward, 2007). The investigation of neurocognitive processes involved in creative idea generation or in divergent thinking (i. e. generating different creative solutions to open-ended problems), and in creative problem solving or insight problem solving can be considered as prototypical examples for research in this field (Benedek & Fink, 2018). The most widely used divergent thinking task (Alternative Uses Task), for example, requires people to generate as many and as original uses for everyday objects. The outcomes measured from such tasks, including ideational fluency (number of generated ideas), flexibility of thinking (number of different categories of ideas), and the originality/novelty of the generated ideas, are considered as reliable estimates of creative potential (Runco & Acar, 2012). Tasks for the assessment of insightful problem solving often require a reframing or restructuring of existing mental representations, which is often associated with the subjective experience of a sudden breakthrough (experience of "AHA"; Bowden et al., 2005; Kounios & Beeman, 2009; Sandkühler & Bhattacharya, 2008). For instance, in the compound remote associates task, three stimulus words are presented (e. g., boot, summer, ground) and participants are required to find a word that forms a compound ("camp") between the three stimulus words (example taken from Bowden et al., 2005).

In the vast majority of neuroscience studies on creativity, brain activity during creative task performance is measured by means of functional magnetic resonance imaging (fMRI) or electroencephalography (EEG). In this particular context, creativity research in the neuroscientific laboratory is often faced with critical task constraints, which make neuroscience studies on creativity often very tricky and challenging. For instance, people are required to be creative while lying supine in a noisy fMRI scanner, or while their heads are wired with electrodes in special electrode caps. Even more importantly, creative activities such as story writing, dancing, painting a picture, or composing a piece of music etc. are not directly transferable to the neuroscientific laboratory. Therefore, studies must decompose a complex, multi-componential creative activity into smaller, more isolated (and thus more measurable) neurocognitive processes that reflect the respective creativity domain to the best possible extent. In the context of dancing, for example, researchers could require their participants to think of an original improvisation dance and compare the resulting brain activity to that measured while thinking of monotonous sequences of movement (e. g., dancing the waltz; Fink et al., 2009). Similarly, since writing or drawing with a pen would hinder reliable fMRI or EEG assessments (artefacts due to motor activity), studies often ask their participants to think of creative ideas in a predefined thinking period, and subsequently to verbally express the ideas generated (Benedek et al., 2019; Fink et al., 2007; Rominger et al., 2018; in Figure 1 an example adopting this procedure is given). The registration and subsequent quantitative and qualitative assessment of responses during performance of the creativity task, is essential to investigate brain activation in relation to creative performance. Benedek et al. (2019) have recently provided a literature overview of how studies successfully meet the manifold constraints imposed by cognitive neuroscience research. In this particular context, studies converged to some common practices and methodological approaches, which have contributed greatly to increase both the reliability of fMRI and EEG assessments, and the reproducibility of findings in the field of creativity. This includes, inspired by the behavioral/psychometric creativity research tradition, the use of empirically-tested and psychometrically-sound experimental tasks for assessing creative cognition in the neuroscientific laboratory (Benedek et al., 2019). Furthermore, in order to avoid contaminations with response-related motor activity, neuroscience studies in the field of creativity use clever paradigms, which isolate the creativity-related processes of interest and also separate the stages of creative thought processes from stages of responding. And finally, studies assess both qualitative and quantitative indicators of creative task performance during EEG and fMRI assessment, facilitating an analysis of the relationship between functional patterns of brain activity and creative performances.

## Neurocognitive Mechanisms Underlying Creativity

Neuroscience research on creativity has provided exciting insights on how the brain produces creative thought (Abraham, 2018). Perhaps the most important finding in this field is the fact that creative cognition is associated with activity patterns in widespread neural networks supporting executive functions (e. g., fluency, flexibility of thinking, inhibition of prepotent responses, etc.), memory processes, internally-focused attention, or spontaneous modes of thought (e. g., Beaty et al., 2019; Boccia et al., 2015; Fink & Benedek, 2014; Gonen-Yaacovi et al., 2013). Essentially, relevant neuroscience findings clearly indicate that creative cognition requires a conglomerate of neurocognitive processes that could be well integrated into "normal" cognition (Benedek & Fink, 2019). For example, envisioning possible improvements to products, requires memory processes to build novel representations of these products, sustained internally-oriented attention to guide active imagination, and vigorous executive control to realize effective and useful task solutions by evaluating/elaborating preliminary thinking results, and by inhibiting prepotent/conventional responses.

Another important finding in this context is that more creative people seem to be characterized by stronger functional connectivity between different creativity-related neural circuits, possibly indicating that higher creative ability is linked with an ability to simultaneously recruit different brain circuits to a greater degree than in less creative people (Beaty et al., 2018a). Specifically, creative thinking has been associated with an increased functional connectivity between default and executive brain networks, potentially reflecting the interplay between generative and evaluative thinking processes (Beaty et al., 2016, 2018b). This is a particularly remarkable finding, as these large-scale brain networks act in opposition in most other cognitive tasks. For example, during goal-directed cognition, such as working memory processing, the executive network exhibits increased activation, while there is deactivation in the default mode network, putatively indicating the attenuation of task-irrelevant mental activity (Anticevic et al., 2012; Beaty et al., 2016). Similarly, Rominger et al. (2019) measured transient phase-locking between neuroelectrical signals at different cortical sites (as introduced in Lachaux et al., 1999) and found that, during the creative thinking process, people who generated more creative ideas showed a more rapid increase in functional connectivity between frontal and parietal-occipital sites, putatively indicating more effective executive processes. This

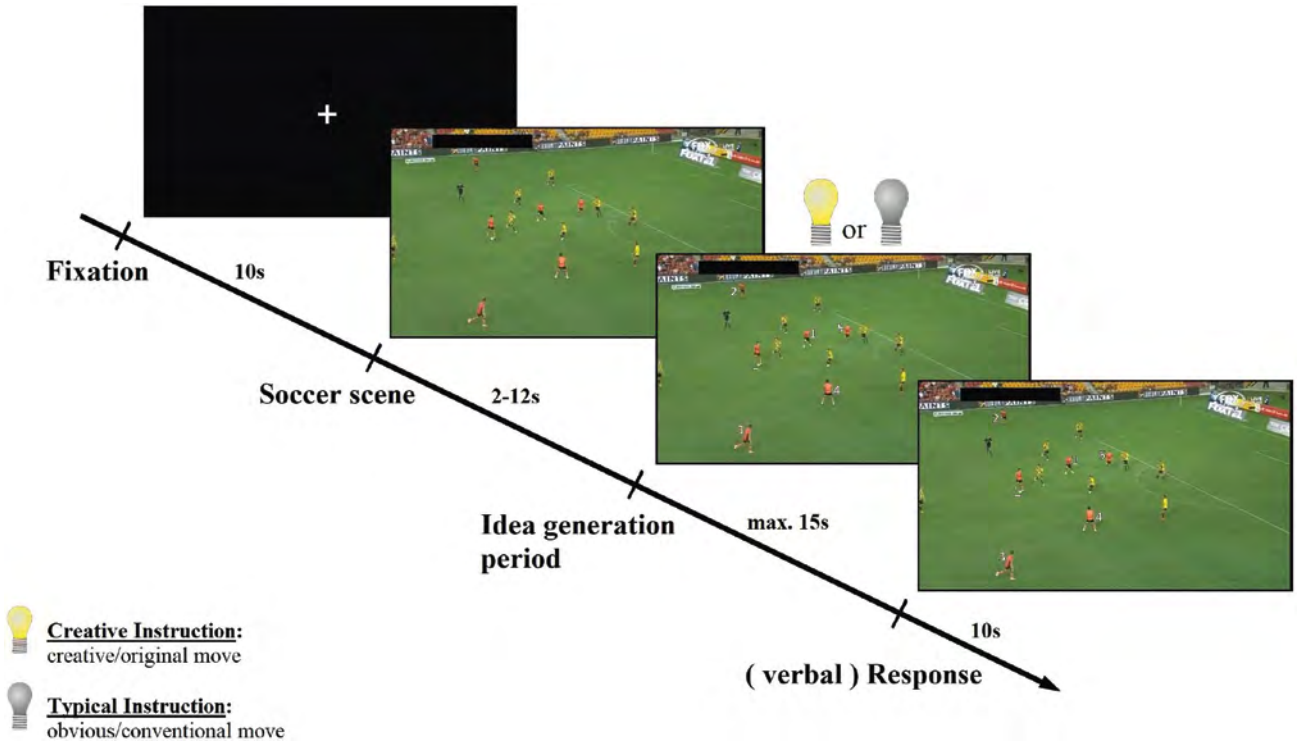


**Figure 1:** Schematic time course of a trial of the soccer decision-making task during EEG and fMRI assessment (taken from Fink et al., 2018; https://doi.org/10.1016/j.neuropsychologia.2018.04.025). A trial started with presentation of a fixation cross for 10 s (assessment of brain activity during a pre-stimulus baseline). Afterwards brief video clips of naturalistic soccer decision-making situations are shown (ranging from 2 to 12 s). During the idea generation period, a fixed image of the soccer scene remains visible on the screen, signalling participants to imagine themselves as the acting player, and, depending on the respective task instruction, to think either of an obvious/conventional (switched off bulb, control condition) or a creative/original move (bulb switched on) while maintaining the target orientation (i. e., scoring a goal) in mind. When a participant thought of a solution/move they were instructed to press the IDEA button, and to vocalize the imagined move (max 10 s; e. g. pass to 1, then pass to 3, etc.). Oral responses were recorded via microphone and transcribed for further analyses.

study adds important evidence to support the notion that temporal dynamics of neuro-cognitive functions across the creative thinking process also affect the quality (i. e., creativity) of the outcome.

## Trends in Research on the Neuroscience of Creativity

Recent studies in the field of creativity and neuroscience are also concerned with the investigation of brain activity patterns during everyday real-life creativity tasks. For example, some studies have investigated brain activity patterns while participants were required to be creative in affective contexts, i. e. to generate reappraisals to self-relevant negative emotional events (Fink et al., 2017; Papousek et al., 2017; Perchtold et al., 2018). Participants were required to generate reappraisals of given anger-eliciting situations (as many and as different as possible), in such a way that reduces anger, which naturally arises when confronted with these scenarios. Cognitive reappraisal is regarded as an effective strategy to cope with adverse events (e. g., Augustine & Hemenover, 2009; Webb et al., 2012), representing a promising, non-pharmacological resource to improve psychological health and well-being (Gross & John, 2003). As in conventional creative ideation, cognitive reappraisal requires the generation of alternative, but useful, and effective solutions to an open-ended problem. It further requires people to flexibly adopt and to generate new perspectives, solutions or strategies, and to override the typical and most obvious responses elicited by this situation (e. g. experience of anger). Such flexible idea production is likewise seen in many other creativity-related tasks, and in fact, both fluency and flexibility of cognitive reappraisal have been found to be significantly and positively associated with conventional divergent thinking measures and with openness, which is closely linked to creativity (Weber et al., 2014). In line with this, neuroscientific findings indicated that cognitive reappraisal was

generally associated with a similar pattern of brain activity as conventional creative ideation (Fink et al., 2017; Perchtold et al., 2018). As expected, some important differences were found between cognitive reappraisal and conventional creative ideation. Specifically, cognitive reappraisal (vs. conventional creative ideation) was associated with a more intense involvement of executive processes, necessary to regulate an ongoing negative emotional state, in addition to processes involved in conventional creative ideation (Fink et al., 2017). Furthermore, Perchtold et al. (2018) found that cognitive reappraisal was, among others, also associated with brain networks implicated in social cognition.

Another example where creativity and neuroscience studies involve real-life demands is research in the athletic domain of soccer. Successful solutions in soccer game situations are often original and surprising. Soccer players need to focus their attention on specific conditions of the soccer scenario (positions of teammates and opponents), to anticipate the behavior of other players, and to think of possible passes or moves that are most promising to score a goal. The imagination of creative moves also involves search and retrieval of task-relevant information stored in memory (e. g., soccer-specific rules, technical knowledge about the execution of a pass or move, trained standard situations, etc.). Additionally, in order to generate a creative and effective move, soccer players are required to evaluate the efficacy and appropriateness of an imagined move, and to inhibit inappropriate, potentially less successful solution approaches. Creative solutions in sport situations thus seem to be characterized by mechanisms that are very similar to those seen in other creativity-related domains (e. g., Rasmussen & Østergaard, 2016; Roca et al., 2018; for overview see Memmert, 2015). Based on these assumptions, some studies have therefore investigated neurocognitive mechanisms associated with creative solutions in naturalistic soccer decision-making situations (Fink et al., 2018, 2019).

In these studies, soccer players (from hobby to amateur) were presented brief video clips of real soccer decision-making situations (ranging from 2 s to 12 s in length). After the image was frozen they were asked to imagine themselves as the acting player of the attacking team, and depending on the respective task instruction, to think either of a creative/original (possible and promising), or an obvious/conventional move (control

condition), that might lead to a goal. Performance of the soccer decision-making task was associated with comparatively strong decreases in EEG alpha power (relative to a pre-stimulus baseline) at parietal and occipital sites, indicating high visuospatial processing demands during the processing of the complex soccer scenarios (Fink et al., 2018). Interestingly, more creative performance in the soccer task was associated with stronger alpha power reduction over left cortical sites, primarily involving motor-related areas. This finding suggests that individuals who generated more creative moves were more intensively engaged in processes related to motor or movement imagery. Similarly, findings from an fMRI study (Fink et al., 2019) revealed that variations in soccer-specific creativity were associated with brain activity in a mainly left-lateralized network of brain regions, which support various cognitive functions such as semantic information processing, visual and motor imagery, as well as the processing and integration of sensorimotor and somatosensory information. Taken together, these EEG (Fink et al., 2018) and fMRI (Fink et al., 2019) studies revealed that imagining creative soccer moves is a complex cognitive process, involving multimodal input from different sensory, motor and perceptual sources. These studies also provide evidence for the notion that neural underpinnings of creativity differ across domains (e. g., Baer, 1998; Boccia et al., 2015). Furthermore, these studies also support evidence from the behavioral research domain, which highlights the crucial role of cognitive and executive functions in successful soccer performance (e. g., Scharfen & Memmert, 2019; Vestberg et al., 2017). Nevertheless, additional research is needed to delineate the manifold neurocognitive processes (e. g. imagery, attention, visual and sensorimotor information processing) implicated in this domain, and to assess how these processes contribute to the generation of creative solutions in soccer.

## Conclusion

Earlier neuroscience studies of creativity have been criticized due to their diversity and inconsistency of findings (Dietrich & Kanso, 2010), showing only "little clear evidence of overlap" (Arden et al., 2010, p. 143). This inconsistency has been traced back to the variegated and multi-componential nature of creativity, as well as to the diversity of methodological approaches used (Fink & Benedek, 2014). However, in the last decade considerable progress in the development of psychometric and laboratory creativity tasks has been made. In fact, neuroscientific studies on creativity have since converged to some common practices and approaches, which have greatly contributed to enhance reliability and reproducibility of findings in the neuroscience of creativity (Benedek et al., 2019).

Recent neuroscience studies on creativity have taken a step further by investigating creativity in more natural settings involving ecologically valid tasks (e. g. creativity in an affective context: Perchtold et al., 2018; creativity in soccer: Fink et al., 2018; or musical improvisation: Bengtsson et al., 2007). Findings therein have suggested some overlap with brain activity patterns during conventional creative ideation and also indicated that creativity and its underlying neural mechanisms are specific to a particular domain (e. g., Boccia et al., 2015; Fink et al., 2018; Rominger et al., 2018). Finally, another exciting trend in the neuroscience of creativity is concerned with approaches to enhance creativity, involving a broad diversity of interventions ranging from cognitively-oriented techniques (e. g., Sun et al., 2016) to interventions of physical activity such as walking (Oppezzo & Schwartz, 2014) or cycling (Colzato et al., 2013). In light of the high plasticity of the brain towards learning or training (e. g. Weber et al., 2019), and given the importance of creativity in almost all aspects of daily life, future creativity research will be particularly challenged to address the question of how creative abilities can be realized to their best possible extent.

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# Bionotes

**Assoz. Prof. Mag. Dr. Andreas Fink**
University of Graz, Institute of Psychology
Universitätsplatz 2/III
A-8010 Graz, Austria
Phone: +43 316 380 8482
Web: https://psychologie.uni-graz.at/en/biological-psychology/
**e-mail: andreas.fink@uni-graz.at**
ORCID ID: orcid.org/0000-0001-7316-3140

Andreas Fink is a psychologist and neuroscientist at the Institute of Psychology of the University of Graz. His research activities include the neuroscience of creativity and approaches to enhance creativity. He also focuses on the relationship between physical activity, cognitive-affective functions and the brain.

**PD. Mag. Dr. Mathias Benedek**
**e-mail: mathias.benedek@uni-graz.at**
University of Graz, Institute of Psychology
Universitätsplatz 2/III
A-8010 Graz, Austria
Phone: +43 316 380 8475
Web: https://psychologie.uni-graz.at/de/dips/team/mathias-benedek/
**e-mail: mathias.benedek@uni-graz.at**
ORCID ID: orcid.org/0000-0001-6258-4476

Mathias Benedek is a psychologist and neuroscientist at the Institute of Psychology of the University of Graz. His research focuses on the neurocognitive mechanisms in creative cognition. Moreover, he is interested in the psychometric assessment of creativity and the role of personality and intelligence in creativity.

**Review Article**

Philipp Kellmeyer*

# Artificial Intelligence in Basic and Clinical Neuroscience: Opportunities and Ethical Challenges

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**Abstract:** The analysis of large amounts of personal data with artificial neural networks for deep learning is the driving technology behind new artificial intelligence (AI) systems for all areas in science and technology. These AI methods have evolved from applications in computer vision, the automated analysis of images, and now include frameworks and methods for analyzing multimodal datasets that combine data from many different source, including biomedical devices, smartphones and common user behavior in cyberspace.

For neuroscience, these widening streams of personal data and machine learning methods provide many opportunities for basic data-driven research as well as for developing new tools for diagnostic, predictive and therapeutic applications for disorders of the nervous system. The increasing automation and autonomy of AI systems, however, also creates substantial ethical challenges for basic research and medical applications. Here, scientific and medical opportunities as well ethical challenges are summarized and discussed.

**Keywords:** big data; deep learning; machine learning; artificial intelligence; neuroethics

**Zusammenfassung:** Die Analyse großer Datenmengen (big data) mit künstlichen neuronalen Netzen für tiefes Lernen (deep learning) ist die treibende Technologie hinter neuen Systemen der künstlichen Intelligenz (KI) für alle Bereiche der Wissenschaft und Technik. Diese KI-Methoden haben sich aus Anwendungen in der automatisierten Bilderkennung (computer vision) entwickelt und umfassen heute Methoden zur Analyse multimodaler Datensätze, die Daten aus vielen verschiedenen Quellen kombinieren, darunter biomedizinische Geräte, Smartphones und allgemeines Nutzerverhalten auf Apps und im Netz. Für die Neurowissenschaften bieten diese zunehmenden Ströme persönlicher Daten und Deep Learning viele Möglichkeiten für die grundlagenorientierte Forschung sowie für die Entwicklung neuer diagnostischer, prädiktiver und therapeutischer Anwendungen bei Erkrankungen des Gehirns. Die zunehmende Automatisierung und Autonomie von KI-Systemen erzeugt aber auch erhebliche ethische, rechtliche und gesellschaftliche Herausforderungen. In dieser Arbeit werden die neurowissenschaftlichen und medizinischen Chancen sowie ethischen Herausforderungen zusammengefasst und diskutiert.

**Schlüsselwörter:** Big Data, maschinelles Lernen, Tiefes Lernen, Künstliche Intelligenz, Neuroethik

***Corresponding author: Philipp Kellmeyer**, Neuromedical Artificial Intelligence Lab, Department of Neurosurgery, Medical Center – University of Freiburg, Engelbergerstr. 21, D-79106 Freiburg im Breisgau, Phone: +49-761-87570; Freiburg Institute for Advanced Studies (FRIAS), University of Freiburg, Germany; Cluster of Excellence BrainLinks-BrainTools, University of Freiburg, Germany; Institute for Biomedical Ethics and History of Medicine, University of Zurich, Switzerland,
e-mail: philipp.kellmeyer@uniklinik-freiburg.de,
ORCID number: 0000-0001-5538-373X

## Introduction

Artificial intelligence (AI) seems to be everywhere now. From navigational tools, digital assistants, and self-driving vehicles, to social robots, autonomous weapons, analytic and predictive tools in science to decision-support systems in medicine and many other domains and applications.

This development is in large parts a result of a particular technological convergence in recent years: the concomitant rise of big data, advanced methods of machine learning (e. g. deep learning) and increasing computing power and efficiency. This perfect technological storm drives a large-scale techno-social transformation across all sectors in society: work, health, research and technology and the social domain; which is often indiscriminately referred to as digitalization.

But what is AI exactly and why does it capture the imagination so vividly and often disquietingly? What is the

current and future impact of AI for neuroscience and the clinical fields occupied with treating brain diseases and mental health disorders? What are the ethical, legal, social and political tensions and challenges that emerge from this techno-social constellation?

Here, I will first provide short and succinct background information on the technological aspects of the current wave of AI methods and contextualize these developments in terms of their putative current and future applications in neuroscience. This will provide the basis to then discuss important ethical, legal and social challenges. The focus in that regard will be on the question of how societies can benefit from the many promising applications of AI in neuroscience and neuromedicine while ensuring the responsible design, development and use of this transformative technology.

## Background: Artificial intelligence, big data, machine learning and neurotechnology

According to the latest analysis of the innovation dynamics of emerging technologies from 2018—the Gartner®[1] Hype Cycle for Emerging Technologies—artificial neural networks (ANNs) for deep learning are currently located at the very "peak of inflated expectations". This represents a snapshot of the cacaphonous media buzz and hype surrounding the putatively transformative power of AI for all sectors of society. As a basis for our discussion here, we need to recognize that the main driving force of what is usually referred to as AI today is the convergence of several technological innovations and components[2]:

- Ubiquitous data-collecting technology: in the environment (e. g. public closed-circuit television), in machines (e. g. cars), in personal devices (e. g. smartphones for collecting personal data on user behavior, movement, geolocation and many other parameters), as well as the traditional arenas in biomedicine such as medical centers and research institutions.
- The, mostly cloud-based, server infrastructure to store and process large amounts of these personal data (big data);
- High-performance analyses on these data with graphics processing units (GPUs), particularly with
- Machine learning (ML) methods, particularly artificial neural networks for deep learning,
- Dynamic user interfaces to facilitate human-AI interaction

These infrastructural and technical components provide the basis for many applications of AI in research, technology development and clinical medicine. One illustrative and highly dynamic translational research area is the field of neurotechnology. **Figure 1** illustrates how many of the components mentioned above can be fully integrated to build an AI-based brain-computer interface that could provide a paralyzed individual with the means to operate a computer-based communication system. But neurotechnology is not confined to the assistive treatment of relatively rare neurological disorders, such as severe paralysis / locked-in syndrome, but has recently also entered the consumer-market with various devices for neurofeedback-based relaxation or well-being applications (Ienca et al., 2018; Kellmeyer, 2018).

## Current and future applications of AI for basic and clinical neuroscience

In neuroscience, as in most other research areas, AI systems based on artificial neural networks have a wide spectrum of applications. As we have discussed, machine learning with ANNs has proven particularly successful in computer vision tasks. Therefore, the primary domain of application in neuroscience will also be the processing and classification of a large amounts of images. Examples are the classification of histopathological images (Litjens et al., 2016), the segmentation of tumors in brain MRI images (Pereira et al., 2016) and many other processing applications in neuroimaging (Akkus et al., 2017; Milletari et al., 2017; Kleesiek et al., 2016). In addition to such computer vision task, however, AI methods based on ANNs are also successfully used in the analysis of bioelectric and hemodynamic brain signals, particularly electroencephalography (EEG) (Schirrmeister et al., 2017a; Schirrmeister, et al., 2017b). In that research area, EEG signal analysis with deep learning could be used, inter alia, to operate an autonomous robot via a brain-computer interface (Burget et al., 2017), classify EEG recordings as normal or pathological (Schirrmeister et al., 2018). Another emerging machine learning method, generative adversarial networks (GANs), have recently been applied in neuroscience to generate naturalistic EEG signals (for data augmentation purposes) (Hartmann et al., 2018), and other applications (Wang et al., 2019).

1 https://www.gartner.com

2 For technical definitions please consult the entries in the Glossary appended here

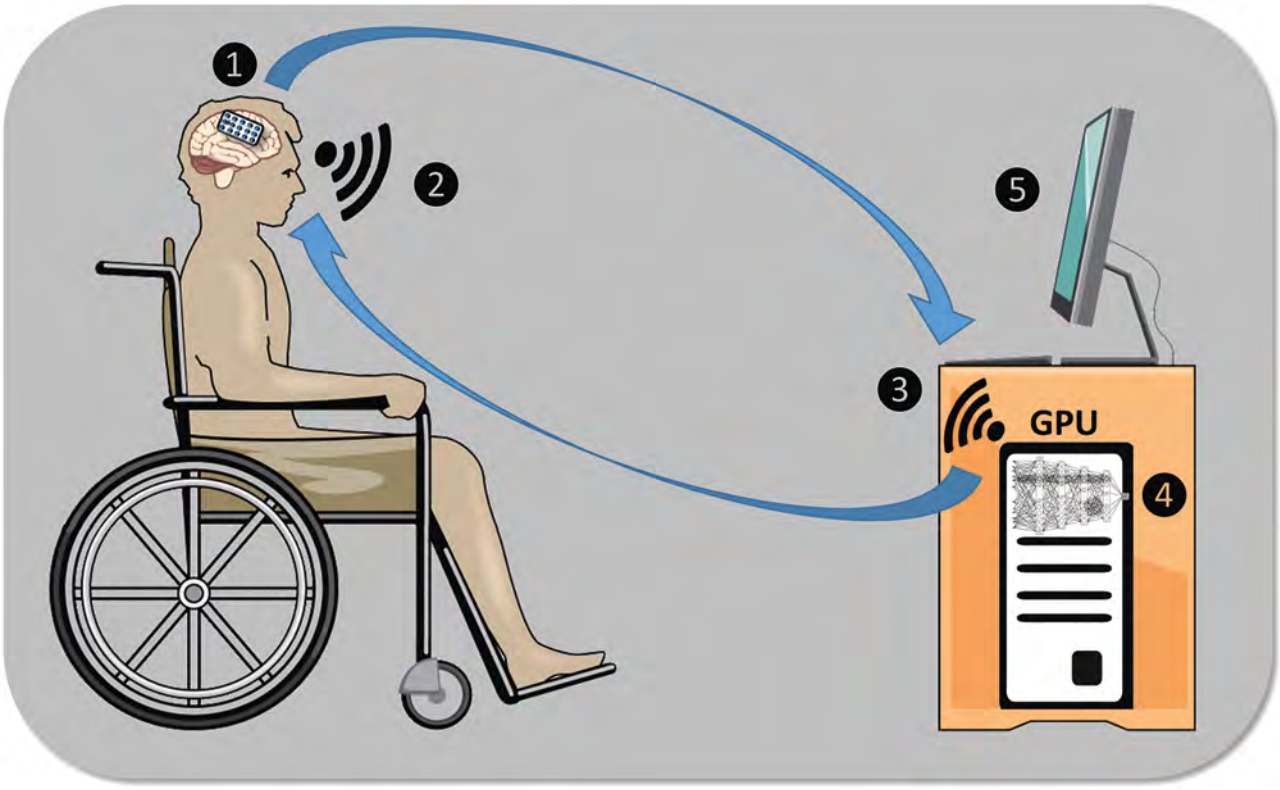


**Figure 1:** Example of an AI-based brain-computer interface that integrates ❶ intracranial electroencephalography (iEEG) to sense bioelectric brain activity and ❷ transmit large amounts of brain data to a ❸ computer-based processing unit with a ❹ high-end GPU that uses deep learning to analyze the brain data which in turn is used to operate a ❺ dynamic user interface, e. g. for communication.

Apart from these applications in data analytics in neuroscience, a comprehensive and high-impact review (Hassabis et al., 2017) of how neuroscientific knowledge and methods can inspire AI methods, and vice versa (Marblestone et al., 2016), has shown that ANNs for deep learning have contributed substantially to the understanding of complex cognitive functions, such as attention, memory and learning, at the level of regional and inter-regional brain networks.

In clinical neuroscience, understood here as the overlapping domains of clinical research and clinical provision in neurology and psychiatry, these AI methods also provide fertile ground for new applications in diagnosing, predicting and treating brain diseases and mental health disorders.

To highlight a few developments here: (a) in the area of diagnostics, the AI-based image processing methods could obviously be used for various groundbreaking applications—e. g. the differentiation between healthy and pathological brain images, the segmentation of tumor tissue from brain MRI images, the diagnosis and sub-classification of neurodegenerative movement disorders from tracer-based imaging. (b) In the area of prediction, the same methods could be used to predict the onset of dementia, or the likelihood / risk of epileptic seizures from implanted cortical electrodes, predict the fluctuations of disabling movement symptoms in Parkinson's disease from deep brain electrodes, and of course many other applications. In the area of therapy, deep learning with ANNs could be used to develop new targeted drugs (Popova et al., 2018; Gawehn et al., 2016)[16, 17], e. g. based on antibodies and fusion proteins ("biologicals"), e. g. for treating neuroimmunological diseases such as multiple sclerosis; or for closed-loop control of impending epileptic seizures via a real-time cortical monitoring and electrostimulation system (Berényi et al., 2012).

The breadth of the actual and potential applications of AI methods can only be sketched here; the reader's imagination is trusted, however, to visualize the full extent and importance of this development for neuroscience and medicine in general, which have also been treated comprehensively by other authors, see e. g. (Topol, 2019). Such a profound and cross-cutting socio-technological change, one might say paradigm shift, of course, creates substantial ethical legal and social challenges, some of which shall be highlighted here.

# Ethical challenges of human-AI interaction in basic and clinical neuroscience

In this section, I highlight some of the most widely discussed current ethical concerns and tensions in neuroethics, neurolaw and related disciplines that engage with these issues. As a disclaimer, given the limited scope here, I neither aim to provide a complete overview nor anything other than my own subjective view on these issues–for a selection of further recent contributions and views please also see (Ienca et al., 2018; Amadio et al., 2018; Illes, 2017; Yuste et al., 2017; Ienca et al., 2017; Mittelstadt et al., 2016).

## Shared agency and autonomy in human-AI interaction

In the context of very close human-AI interaction, for example in a closed-loop brain-computer interface in an epilepsy patient, the degree to which the underlying AI system is granted decision-making capacity and—conversely—how much the human subject is kept in the loop in these interactions may lead to new hybrid forms of human-machine or human-AI actions.

Imagine, for example, Maria, a 45 year old woman with severe motor paralysis of the upper and lower limbs who has been implanted with a closed-loop electrode system that allows her to use her brain activity to operate a service robot that can reach, grasp and bring her objects.

Now, any particular action sequence by Maria, say for example fetching a cup and drinking tea, is only realizable by decoding her brain activity and having the robot perform the required tasks. Suppose further that the robot itself also has some degree of autonomy in terms of how it realizes this goal, for example it may have the capacity to freely roam the room and grasp the cup any way that is optimal for realizing the set goal. In such a scenario, it would be reasonable to consider the human-robot interaction necessary for realizing Maria's goals as requiring a form of shared agency (and autonomy) between Maria and the service robot.

This may seem perfectly fine for all instances in which the interaction works as intended by Maria and her goals a fully realized without significant deviations from the robot. But what happens in cases of unintended yet substantial failures—what if, for example, the robot spills the hot tea and injures a third person or Maria herself? Such interactions gone awry lead to questions of responsibility and accountability in human-AI interaction that are difficult to navigate both ethically and legally.

## Accountability, responsibility and the question of trust

Without having the space to provide a detailed and philosophically grounded conceptual analysis here, I urge the reader to consider the difference—ethically and legally—of the concepts of accountability and responsibility. Both denote the ascription to an individual (or active claim by an individual) of some kind of causal agency in a particular action or sequence of actions; for example: "Margret was responsible for writing the letter to the president." or "The policeman is accountable for explaining his use of his service weapon.".

In cases of very close, shared or even hybrid actions that are performed in concert by a human and an AI system, however, one might encounter a gap in our ability to unequivocally ascribe responsibility and/or accountability to particular actions. This "accountability gap" (Kellmeyer et al., 2016) may arise in many situations in which decision-making capacity is relegated to an AI system—e. g. a deep-learning-based brain implant or a self-driving car—whose internal learning dynamics and decision-making processes we cannot sufficiently infer: the so-called "black box" aspect of AI (Castelvecchi, 2016). In the ethical and legal domain, we do not yet have effective and resilient norms to ascribe (let alone adjudicate) responsibility in cases of system failures for such black box systems.

Therefore, the topic of → interpretability of machine learning algorithms, particularly ANNs for deep learning, is not only of great interest for computer scientist and engineers, but also an indispensable prerequisite to be able to provide a reasonable ethical understanding and precise legal instruments to adjudicate future cases of liable human-AI interactions.

## Intrusive AI and the protection of brain data, mental privacy and personal identity

Today, our methods for observing brain activity, mainly EEG, functional MRI and related methods have inherent limit in the ways in which they can measure the temporal, spatial and frequency-related characteristics of brain signals. This limits the amount and quality of information that we can extract from these signals with our current

analytical methods, yet we already see how emerging machine learning methods, specifically deep learning, improve our information extraction capabilities substantially (Akkus et al., 2017; Milletari et al., 2017; Schirrmeister et al., 2017a).

If this progress in data analysis will be complemented by substantial improvement in our measurement methods, for example with intracortical microelectrode grids that measure EEG directly from the cortical surface or, as yet unproven methods such as "neural dust" (a system of intracortical nanoparticles and ultrasound) (Neely et al., 2018), we can expect substantial further progress in the types and amounts of information that can be extracted from neurotechnological measurements.

The practical limits on the amount and specificity of information that can be extracted from brain signals at the individual level—now and in the near future—mean that scenarios involving "reading" the "mind" or "thoughts" will remain elusive for the time being. This will not deter scientists in public (or private-public) research institution nor researchers in technology companies (that have invested substantially in their own neuroscience and neurotechnology research in recent years (Kellmeyer, 2018; Strickland, 2017; Regalado, 2017; Clark, 2017), however, to use brain data as an interesting class of personal data in multimodal deep learning analysis frameworks. In this scenario, we do not yet know whether: a) the *combination* of many different classes of data (e. g. user behavior, geolocation data, data from devices, brain data etc.) allows for hitherto unprecedented inferences on an individual's first-person subjective (i. e. "mental") experience and/or her personal identity (Kreitmair et al., 2017); or, b) the *aggregation* of such multimodal data from an unprecedented number of individuals (e. g. in a large-scale "experiment" on an internet platform in which a company outfits thousands of users with a consumer neurotechnology device, e. g. a dry-cap EEG, for measuring and uploading brain data to their company servers) would allow to identify particular groups of individuals based on social, biological or other markers—which would raise concerns regarding the protection of group privacy (Ienca et al., 2018; Taylor et al., 2017).

In the neuroethics community and other research fields, these concerns have precipitated a discussion around whether brain data should be treated as a special class of data that needs extra protection in data protection guidelines and regulations (such as genetic data e. g.) (Kellmeyer, 2018), perhaps even "neurorights" that refer to basic human rights (Ienca and Andorno, 2017), or whether in fact the question of what actually constitutes biomedical or health-related data becomes increasingly meaningless as AI methods can make health-related inferences on many different types of data (and their combination and aggregation) that would have previously not been considered to be special health-related data (e. g. your movement patterns from your mobile phone, or your user behavior on the web).

## Bias in human and artificial intelligence in interaction

The propensity to take "mental shortcuts" (also known as a → heuristic) for judgement is an inherent feature of human cognition and serves important purposes in everyday life decision-making. If these heuristics, however, produce systematic skews in our decision-making, they are called biases which, if accumulated over time, can produce substantial distortions of knowledge and behavior both at the individual and societal level. These individual and societal biases are also an important driver of creating and maintaining social injustices, e. g. rooted in prejudice, stereotyping, discrimination and other negative social attributions.

The data streams that power current large-scale AI systems, e. g. in translation engines, navigation systems or computer vision (e. g. face recognition technology) today are based on human-derived knowledge structures (ontologies) and most artificial neural networks for deep learning are trained with data that require the input of human experts (e. g. for selecting and labeling the data). Therefore, any bias that is engrained at the level of data selection, structuring, labeling and so forth, may be reproduced, inflated and disseminated by an AI system that is trained on these biased data. Many examples in recent years show, how this can lead to a perpetuation of social injustices and discriminations that are based on human biases, e. g. with respect to ethnicity, gender and other social markers (Knight, 2017; Baeza-Yates, 2016).

Now, there is no easy fix for this deeply entrenched and interlocked problem of human biases and their spillover effects into AI bias. For one, human cognitive biases are almost impossible to contain effectively at the individual level, i. e. most behavioral training methods for so-called de-biasing have failed to show substantial let alone sustainable effects in reducing cognitive biases in humans (Smith and Slack, 2015; Croskerry et al., 2013a; Croskerry et al., 2013b). Furthermore, there is also no straightforward way computationally to effectively de-bias AI systems, both in terms of reducing the technical aspect of bias in algorithms (see → bias) nor the human-derived biased data structures and ontologies (Krywko, 2017; Geman et al.,

1992). On the bright side, many computer scientists and data scientists have now recognized the problem and are actively working on potential ways to mitigate the problem (Courtland, 2018).

Meanwhile, however, it is important for researchers in neuroscience and clinicians to be aware (and to raise critical awareness) that automated AI systems may contain biases in their decision-making procedures.

### The problem of "perpetual ethics", governance of AI systems and fair access

In the legal, political and regulatory sphere, these developments raise questions on whether existing regulatory and legal procedures suffice for ensuring the responsible research and effective governance of AI across all sectors in society, while preserving the innovation dynamics of the beneficial applications of this emerging technology (Voeneky and Neuman, 2018; Kaebnick et al., 2016)[42, 43]. Raising awareness and promoting a participatory societal discourse on the ethical issues around AI is commendable and necessary first step for achieving a more inclusive process of deliberation and technology governance.

At the same time, however, the inherent complexity of human-AI interaction and the many stakeholders in AI could also produce a potential problem of "perpetual ethics"—an infinite loop of inter- and transdisciplinary debate without a mechanism and route for democratically legitimized and evidence-based sociopolitical adaptations in the form of laws, rules and regulations.

We can already see how the big five technology companies are all too eager to participate in (some might say usurp) the ethical discourse around AI and neurotechnology (Murgia and Shrikanth, 2019; Hoffmann, 2017). A democratically grounded process of multistakeholder deliberation on the ethics of AI and neurotechnology, however, requires equal and fair access to the debate in the public sphere, rather than the oligopolization of ethical discourse by academia, experts and big companies. Importantly, researchers of all career levels involved in AI-related disciplines (whether from a developmental, computer science perspective or in applied areas such as medicine) can actively participate in exerting counterpressure to this domination of the ethical discourse by private companies by engaging in science communication and public outreach at their institutions.

Furthermore, apart from this bottom-up process of a participatory discourse in societies on equal terms, the transnational nature of technology governance also requires the involvement of supranational bodies (such as the EU) and international organizations (such as the UNESCO) in developing effective and adaptive instruments of governance (i. e. laws and regulations) that preserve the right and freedom to science while making sure that AI is used to nurturing human well-being and flourishing rather than feeding the revenue stream of big technology companies.

## Conclusions and outlook

The comprehensive technological change associated with big data, deep learning and the expansion of the digital infrastructure offers many reasons to hope for groundbreaking progress in basic and clinical neuroscience.

At the same time, neuroscience and neurotechnology, as academic and professional fields, should actively work towards embedding and integrating research and conceptual analysis on the ethical tensions in human-AI interaction into their activities. Basic ethics curricula, at all levels of secondary education, in all professions engaged in neuroscience and neurotechnology research and development, should become the norm rather than the exception. We need the coming generations of neuroscientists, programmers, engineers and other specialists to add ethical thinking and analysis into to their methodological toolbox and professional capabilities.

To this end, the comparatively young academic fields of neuroethics (Kellmeyer et al., 2019) and neurolaw (Meynen, 2014) are emerging as particularly dynamic (and partly overlapping) research and teaching environments for addressing the manifold ethical, legal and social challenges from human-AI interaction in the arena of neurotechnology and neuroscience.

Ultimately, from a professional perspective, the engagement with the profound ethical challenges that are created by large-scale techno-social transformations such as AI (or gene editing) is not only adding value to our identity as researchers and/or clinicians in neuroscience but may, collectively, mitigate negative consequences of this rapid change for society.

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# Glossary

**Algorithm**: Very generally, an algorithm is a procedure (e. g. a computation) for solving a particular problem by following a set of instructions step-by-step. In order to function properly important features of algorithms are that: the set of instructions must be definite and without contradictions; each step must be realizable; the description must be finite; the final step should produce a result; it should be determinate in the sense that when repeated under the exact same circumstances the result of the procedure should be the same and that at any given step in the procedure, there is only one option to proceed.

**Artificial Intelligence (AI)**: Artificial intelligence is an umbrella term that has many different definitions that to some degree also depend on the goals that an AI system is designed to achieve. Most commonly, it refers to a subfield of computer science that aims at creating computer programs that can perform tasks that under usual circumstances would require human intelligence; e. g. speech perception, facial recognition, navigation, or other tasks.

**Artificial Neural Networks (ANN)**: In the field of → machine learning, an artificial neural network is a computing program architecture that is inspired by the structure of neural networks in animal brains. An ANN in its most basic form consists of different layers of interconnected units (called nodes or artificial neurons)—e. g. an input layer, intermediate layer and output layer. The artificial neuron receives an input (a real number), performs a computation (using a non-linear function) and thus creates "weights" which can be used in various forms of learning. The performance of an ANN depends, among other factors, on the quality of the input data, the number of intermediate layers, the degrees of connectedness between the nodes and the type of learning scenario (e. g. reinforcement learning).

**Bias**: In everyday language, bias refers to systematically skewed decision-making that is often associated with discrimination and other forms of unfairness. More systematically, e. g. in the field of psychology, a cognitive bias refers to a systematic tendency in human decision-making that skews decisions in a particular way (Tversky and Kahneman, 1975). One example, from the groundbreaking work on cognitive biases by the Israeli psychologists Tversky and Kahneman, would be the "availability bias", i. e. the tendency to use information that is readily at hand for judgement (rather than including information that needs some sourcing). Cognitive biases can be a useful and adaptive → heuristic under circumstances that require rapid action but may equally be maladaptive or irrational in situations that require deeper deliberation or reflection.

In → machine learning and statistics, in contrast, bias refers to the difference between a calculated expected estimate (or value) of a parameter and this parameter's true value.

**Big Data**: There is no universally accepted definition on what parameters qualify a particular data set to be considered "big data" (Mauro et al., 2015). An early definition, still in use today in some form or another, by the technology consultancy Gartner® emphasized the aspects of "high-volume, high-velocity and/or high-variety information assets" (Gartner, 2003) as being characteristic of big data sets.

**Black Box (aspect of AI / Deep Learning):** The black box aspect of AI is a concern which is often invoked in discussions around questions of opaqueness, transparency and → interpretability of → deep learning (and some other AI methods). Usually it refers to the inability to retro-infer the information content and processes that have occurred in a trained deep neural network. One reason is that, unlike your computer's random access memory (RAM), information in deep neural networks is diffused throughout the layers and nodes that makes it next to impossible to extract. In analogy to the brain, information storage in ANNs is reflected in the strength of the connected units rather than in any particular set of nodes or layers. Many computer scientists are now working on opening this black box, but no general solution has been developed to the problem yet (Castelvecchi, 2016).

**Brain Data**: Data on the structure or function of the brain and its various components (networks, cells etc.), examples are MRI images, EEG recordings and other data types.

**Convolutional Neural Network**: A particular class of → artificial neural network based on deep learning (also: "deep neural network") that is inspired by the connectivity patterns in the visual cortex. In a convolutional network, each node (a.k.a "neuron") in one layer of a multilayer network is fully connected to all other nodes in the next layer.

**Deep Learning**: A → machine learning method in which an → artificial neural network (in that case also referred to as a "deep neural network") with many dozens to hundreds of layers is used for data analysis

**Emerging Technologies**: General term that refers to technologies that have been demonstrated to function in a particular way, but are not yet fully developed and/or realized and are typically not available in the market place on a large scale. Current examples would be self-driving cars or brain-computer interfaces.

**Generative Adversarial Networks (GANs)**: A → machine learning method in which two → artificial neural networks contest with each other. One network, the generative network, produces data structures, for example human faces, and the other network, the discriminative network, evaluates the output with regard to certain set specifications (e. g. whether the faces resemble faces of famous people on which the discriminator network has been trained with large amounts of data). The generative network produces data (faces) until the discriminator network is unable to distinguish between real faces (that it has been trained on) and generated faces. This method is a powerful tool for increasing the amount of data for training neural networks (data augmentation) but can also be used to produce fake content such as images or videos ("deep fakes").

**Governance**: The process of governing (by supranational bodies, regional or local authorities) a particular social organization unit or social system, e. g. a state, territory or community, via laws, regulation and power.

**Graphics Processing Unit (GPU)**: Parallelized circuits that are specialized for graphics and image processing and are generally more efficient than conventional centralized processing units (CPU).

**Heuristic**: In cognitive psychology, a heuristic describes a method for problem-solving, e. g. by an individual, that relies on immediate and highly automated patterns and/or actions, for

example the application of guesses, "rule of thumbs" or other types of intuitive judgments.

**Interpretability (of → Machine Learning)**: The ability to correctly interpret the results of a machine learning analysis, both in terms of the distinctive classes or features that the machine learning program has produced when analyzing the data.

**Machine Learning (ML)**: The most widely used description of machine learning is "learning without being programmed", which points to the fact that methods used for machine learning at the most general level of description enable a software / algorithm to discriminate patterns in data and/ or make predictions by learning distinctive features from these data that are not part of the original set of programming instructions. There is now an ever growing variety of machine learning methods, of which → artificial neural networks for → deep learning are the most popular and successful in recent years.

**Persuasive Technologies**: A concept from human-technology interaction studies in which technologies by virtue of their particular design features and functions may make the interaction very persuasive for humans. Persuasiveness can have a positive connotation, in the sense that a device's design enables a compelling and intuitive user experience, but can also be perceived as negative, in the sense of being overly manipulative or even deceptive (Fogg, 2003).

**User Experience Design**: An interdisciplinary research field at the intersection of industrial design, psychology and cognitive science that studies human-technology interaction from a user-centered perspective.

**User Interface**: A graphics display or other type of output device that lets a user interact with a computer system. It can have different features such as being static, dynamic, touch sensitive, or adaptive.

**Technological Solutionism**: The societal tendency to turn to technology first, rather than sociopolitical actions say, for solving complex problems in the social realm (Morozov, 2014). Examples would be to respond to shortages in human caregivers by implementing a large-scale program for care robots or to combatting social isolation and loneliness in elderly people with a program of free virtual reality headsets (with an accompanying virtual platform for online interaction).

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# Bionote

**Philipp Kellmeyer**
Neuromedical Artificial Intelligence Lab, Department of Neurosurgery, Medical Center – University of Freiburg, Engelbergerstr. 21, D-79106 Freiburg im Breisgau, Phone: +49-761-87570
**e-mail: philipp.kellmeyer@uniklinik-freiburg.de**
ORCID number: 0000-0001-5538-373X

Dr. Philipp Kellmeyer is a board-certified neurologist at the University Medical Center Freiburg, Germany. He studied medicine at the Universities of Heidelberg and Zurich and received a Master of Philosophy from the University of Cambridge (UK) on a full scholarship. He currently works as a clinical neuroscientist on a brain-computer interface to restore communication in severely paralyzed neurological patients. He is also a scientific member of the Cluster of Excellence ("Exzellenzcluster") BrainLinks-BrainTools, an interdisciplinary research consortium on neurotechnological research at the University of Freiburg. In his neuroethical work he is particularly interested in the ethical challenges of emerging neurotechnologies, applications of big data and machine learning in clinical neuroscience, as well as ethics issues in disorders of consciousness and neurodegenerative diseases. He is also an affiliated researcher at the Institute for Biomedical Ethics and History of Medicine at the University of Zurich where he also teaches biomedical ethics. He is the leader of the Emerging Issues Task Force of the International Neuroethics Society and member of the Advisory Committee of the Neuroethics Network. In 2017, he received the "Förderpreis Bioethik" (Bioethics Prize) of the MTZ-Foundation for his neuroethics work. Since 2018, he is a member of the research focus "Responsible Artificial Intelligence" and Internal Senior Fellow at the Freiburg Institute for Advanced Studies (FRIAS) at the University of Freiburg.

**Review Article**

Shokoufeh Khakipoor, Maxim A. Drömer, Daniel A. Cozetto, Simone Mayer*

# Single-cell RNA-Sequencing in Neuroscience

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**Summary:** Technical innovations in the last decade have allowed to sequence transcriptomes of single cells. Single-cell RNA-sequencing (scRNA-seq) has since then opened the window to a deeper understanding of cellular identity and is becoming a widely used method in molecular biology. In neuroscience, scRNA-seq has broad applications, for example in determining cellular diversity in different brain regions and in revealing transcriptomic variations across brain disorders. The method consists of several steps: isolation and lysis of single cells, reverse transcription of RNAs, amplification of cDNAs, and next-generation sequencing. The large datasets can subsequently be analysed using different bioinformatic tools to deduce biological meaning. Current developments aim to integrate scRNA-seq into cellular network analysis through multimodal analysis, spatial localisation and perturbation experiments, in order to understand brain physiology and pathology.

**Keywords:** Transcriptome, diversity, network integration, neurological disorder, bioinformatics

**Zusammenfassung:** Durch technische Innovationen wurde es in den letzten zehn Jahren möglich, das Transkriptom einzelner Zellen zu sequenzieren. Die Einzelzell-RNA-Sequenzierung (scRNA-seq) liefert ein tieferes Verständnis der zellulären Identität und ist inzwischen eine Standardmethode der Molekularbiologie geworden. In den Neurowissenschaften wird scRNA-seq beispielsweise zur Bestimmung der zellulären Diversität verschiedener Hirnregionen und zur Analyse transkriptomischer Variationen bei Hirnerkrankungen angewandt. Die folgenden Schritte sind nötig: Isolierung und Lyse einzelner Zellen, reverse Transkription von RNAs, Amplifikation von cDNAs und Next-Generation-Sequenzierung. Die Datensätze werden anschließend mit bioinformatischen Methoden analysiert, um sie zu interpretieren. Aktuelle Entwicklungen zielen darauf ab, scRNA-seq durch multimodale Analyse, räumliche Lokalisierung und Störungsexperimente in die zelluläre Netzwerkanalyse zu integrieren, um Neurophysiologie und -pathologie besser zu verstehen.

**Schlüsselwörter:** Transkriptom, Diversität, Netzwerkintegration, neurologische Erkrankungen, Bioinformatik

## Introduction

The physiological, morphological, and molecular properties of an individual cell define its role in neural networks. Molecular properties contribute to physiological and morphological features and can be determined in high throughput by analysing the global ensemble of mRNA transcripts, also known as the transcriptome. For many years, analysing the transcriptomes of specific brain regions was made possible through microarrays and bulk transcriptomic analysis (Figure 1A). These studies have been extremely informative, for example, in revealing transcriptomic differences between brain regions, biological states, or healthy and diseased tissue samples. However, bulk RNA sequencing requires homogenization of entire tissue samples, masking differences between cells. Addressing cellular diversity is crucial for understanding the brain, where dozens of cell types are found in close proximity. In 2009, the first single-cell RNA-sequencing (scRNA-seq) protocol was developed (Tang et al., 2009). Since then, scRNA-seq has transformed several research fields rendering it an essential tool in modern molecular biology. In this review, we aim to introduce the technical foundations of scRNA-seq and highlight some of its applications in basic and translational neuroscience research. In doing so, we hope to orient those new to the field and also those eager to start planning scRNA-seq experiments.

***Corresponding author: Dr. Simone Mayer,** Eberhard Karls University Tübingen, Hertie Institute for Clinical Brain Research, Otfried-Müller-Str. 27, 72076 Tübingen, Germany, e-mail: si.mayer@uni-tuebingen.de
**Dr. Shokoufeh Khakipoor,** Eberhard Karls University Tübingen, Hertie Institute for Clinical Brain Research, Otfried-Müller-Str. 27, 72076 Tübingen, Germany, e-mail: shokoufeh.khakipoor@uni-tuebingen.de
**Maxim A. Drömer,** Eberhard Karls University Tübingen, Hertie Institute for Clinical Brain Research, Otfried-Müller-Str. 27, 72076 Tübingen, Germany, e-mail: maxim.droemer@student.uni-tuebingen.de
**Daniel A. Cozetto,** EEberhard Karls University Tübingen, Hertie Institute for Clinical Brain Research, Otfried-Müller-Str. 27, 72076 Tübingen, Germany, e-mail: dan.cozetto@gmail.com

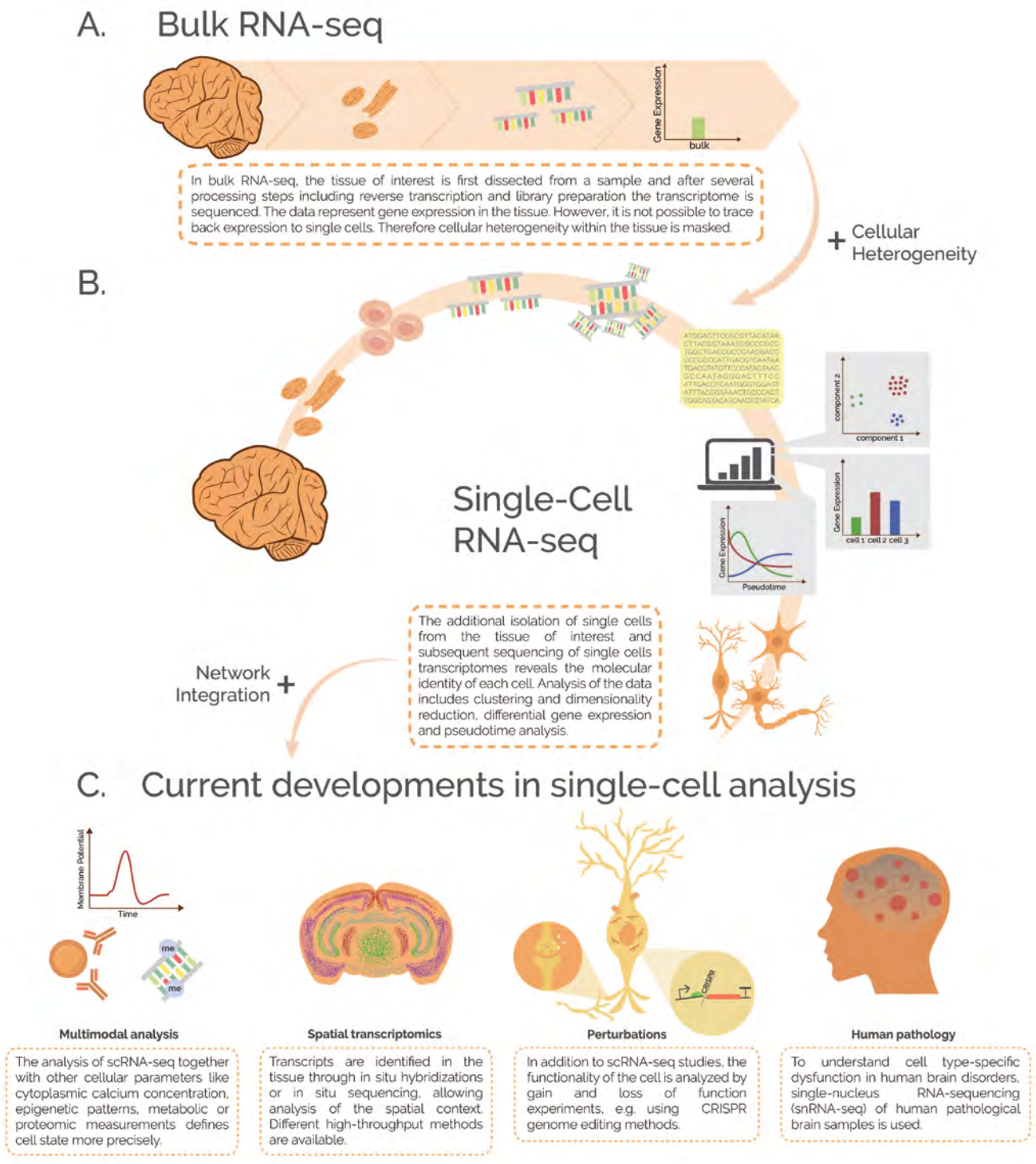


**Fig. 1:** Overview of the development of scRNA-seq in the last decade. (A) Overview of Bulk RNA-seq workflow, (B) overview of single-cell RNA-seq workflow, (C) schematic of current developments in single cell analysis.

# Technical basics: Single-cell RNA-Sequencing Workflow

Over the past decade, scRNA-seq has undergone a process of commercialisation and diversification (Chen et al., 2019; Hwang et al., 2018; Lafzi et al., 2018). Here, we will discuss the basic steps shared by all methods (Figure 1B), an understanding of which is essential when selecting a method for one's own experimental question.

## 1 Dissociation

Single cells are isolated from their tissue context, removing their contacts to each other and the extracellular matrix. A combination of mechanical and enzymatic strategies is used to generate a single-cell suspension (Hedlund and Deng, 2018). Depending on the experimental question, in some studies, authors also include fluorescence activated cell sorting (FACS) in order to isolate cell populations of interest. The isolation of neural cells can be especially challenging due to their high degree of connectivity in networks and their complex morphologies. Therefore, locally translated dendritic and axonal RNAs may be lost (Cajigas et al., 2012).

Additionally, stress induced by dissociation and FACS may influence gene expression leading to upregulation of immediate early genes and heat shock proteins introducing technical artifacts (van den Brink et al., 2017). Dissociation protocols may be adapted to reduce stress, for example, by a transcription inhibitor (Hrvatin et al., 2018; Wu et al., 2017). Alternatively, transcriptomes can be determined from frozen tissue samples through extraction of single nuclei (snRNA-Seq) (Grindberg et al., 2013; Habib et al., 2016; Lacar et al., 2016).

## 2 Single-cell capture

Single cells can be captured using different methods that are characterized by specific advantages (for a comprehensive review on this topic, see (Wang et al., 2019)). In short, three main systems are commercially available: microfluidics (e. g. Fluidigm C1, (Pollen et al., 2014)), nanowell-based system (e. g. Clontech iCell8 (Goldstein et al., 2017)), and nano-droplets (e. g. 10x Genomics (Klein et al., 2015; Macosko et al., 2015)). 10x Genomics is currently widely used due to its high throughput of several thousand single cells analysed per experiment.

## 3 Preparation for the sequencing

After capturing single cells, cells are lysed, and reverse transcription of the RNA is performed. Oligo (dT)-primers are used to generate cDNA of all poly-A-tagged RNA, which is then further amplified through different PCR reactions. Amplification by PCR may cause bias as the exponential amplification distorts the frequency of transcripts towards shorter and GC-rich templates. Finally, sequencing libraries are produced by adding adapters at the 3' and the 5' end of the cDNA for subsequent Next Generation Sequencing (most commonly Illumina Sequencing).

## 4 Bioinformatics analysis

The raw sequencing data is processed and analysed using bioinformatics tools to extract meaningful biological information (AlJanahi et al., 2018; Chen et al., 2019; Hwang et al., 2018; Luecken and Theis, 2019; Nguyen and Holmes, 2019). While there is ongoing development, open-source software packages, including Seurat (Butler et al., 2018) and Scanpy (Wolf et al., 2018) (written in R and Python programming language respectively) provide a good starting point for such analyses. First, sequencing reads are mapped to the genome, and quality control measures are implemented (AlJanahi et al., 2018; Luecken and Theis, 2019). The data is high dimensional since every gene in each cell has a specific expression value, thus making analysis mandatory for biological interpretation. In clustering approaches, cells with similar gene expression are grouped in clusters and mapped to known cell types through marker gene expression (Chen et al., 2019; Hwang et al., 2018). As these clusters appear in high-dimensional spaces, it is not possible to visualise them without dimensionality reduction (Nguyen and Holmes, 2019). Simple projections onto certain coordinates lead to loss of information about similarity, which is often better preserved by more complex projections such as t-stochastic neighbour embedding (t-SNE) which provides two-dimensional plots as shown in Figure 1B (van der Maaten and Hinton, 2008). As these transformations condense information from the original data, it is crucial to interpret with caution. An alternative analysis strategy is to investigate the progression of cell types in a lineage or a disease pathology with pseudotime analysis where an emphasis is put on the continuity of cell states in the population (Hwang et al., 2018).

Due to the various artifacts that can be introduced in any of the steps from dissociation to bioinformatics analysis, validation by orthogonal methods is crucial. Valida-

tion can be performed for example through qRT-PCR, *in situ* hybridization or immunohistochemistry approaches in the tissue, or functionally through perturbation experiments.

# Applications in basic neuroscience research – atlasing and beyond

scRNA-seq has been used to address diverse questions in basic neuroscience. For instance, scRNA-seq has been used to catalogue cell types in different brain areas (Mayer et al., 2018; Nowakowski et al., 2017; Zeisel et al., 2015).

The successful use of scRNA-seq in characterising all cell types in a tissue on the molecular level has led to the initiation of the Cell Atlas, a global effort aiming to catalogue all the cells in the human body including the brain through scRNA-seq (Regev et al., 2017). Current efforts are seeking to mimic human brain development and physiology *in vitro* through the generation of organoids (Kadoshima et al., 2013; Lancaster et al., 2013; Pasca et al., 2015). The characterisation and benchmarking of organoid protocols has heavily relied on scRNA-seq since this method allows the molecular analysis of cells in a heterogeneous tissue (Camp et al., 2015; Pollen et al., 2019; Velasco et al., 2019).

In most studies, transcriptomic findings remain to be linked to the physiological function of cells. One study has already demonstrated the power of scRNA-seq by showing transcriptomic responses to light exposure in dark-reared mice in all cell types, including those associated with the vasculature (Hrvatin et al., 2018). In another study, scRNA-seq has revealed cell-type-specific responses to morphine treatment and revealed substantial changes in glial cells (Avey et al., 2018). Further research on short and long-term consequences in gene expression in response to external stimuli will contribute to a deeper understanding of neural plasticity and learning processes.

# Current developments in single-cell analysis

New technologies have been developed in order to integrate single-cell transcriptomics into traditional methods allowing the implementation of more complex experimental designs (Figure 1C). Here, we highlight recent developments that integrate scRNA-seq into other experimental approaches.

## Multimodal analysis

One criticism of scRNA-seq is that the transcriptome is an incomplete proxy of cell type or cell state. Instead, cellular classification by other features that are more permanent such as the epigenetic landscape, or have a more direct functional importance, such as the proteome, would be preferable. In the last years, several developments have started to enable multimodal analysis, which means that more than one molecular feature is analysed at the single-cell level in high throughput. Now methods are becoming available to combine the transcriptome with the epigenome (Lake et al., 2018) or the proteome (Schenk et al., 2019). Additionally, it is possible to analyse intracellular signalling cascade activation, together with the transcriptome in fixed cells (Gerlach et al., 2019).

## Integrating physiology with scRNA-seq

Neuronal cells are organized in networks in order to realize complex behaviours and cognitive tasks. The individual physiological properties of a neuron are thus of great importance for its function. For a comprehensive understanding of neuronal function, combining electrophysiological recordings with scRNA-seq is therefore essential. In 2016, this feat was first achieved by combining patch-clamp recordings with scRNA-seq through the aspiration of the cytoplasm after the electrophysiological recordings and subsequent transcriptome analysis (Cadwell et al., 2016; Fuzik et al., 2016). This approach, called Patch-seq, combines classical physiological recordings with scRNA-seq as well as connectivity and morphology in intact tissue slices with low throughput (Pfeffer and Beltramo, 2017).

Traditionally, intracellular calcium levels are used as an indicator of neuronal activity and can be measured at single-cell resolution in tissue slices or live animals in order to examine activity in many cells in a neuronal network at the same time (Rochefort et al., 2008). Making use of a classical calcium indicator, we have recently developed an approach, where we combine calcium imaging with transcriptome analysis in dissociated cells using a microfluidic system (Mayer et al., 2019). Combining calcium imaging and scRNA-seq has allowed us to reach a higher throughput (approximately 30 cells per experiment or day) than Patch-Seq (Mayer et al., 2019). Moreover, the analysis of dissociated single cells has allowed us to analyse cell-autonomous physiological responses that do not rely on network activity. Our technique thus provides an example of multimodal single-cell analysis, where we monitor several cellular features, namely the responses to

six different neurotransmitter receptor agonists and the single-cell transcriptomes at the same time (Mayer et al., 2019). We found that analysing physiological and molecular properties of single neuronal progenitor cells or immature neurons at the same time allowed us to gain a better understanding of the functional importance of transcriptomic cell type differences (Mayer et al., 2019). Further developments in this field will allow the integration of calcium imaging with scRNA-seq in the tissue context (Liu et al., 2018), thus integrating scRNA-seq with systems neuroscience.

### Spatial transcriptomics

Spatial transcriptomic methods that determine RNA content in cells while preserving the tissue location have been developed in order to prevent dissociation biases and may also allow subsequent analysis of proteins through immunohistochemistry. There are several protocols available, some also commercially, which each come with their strengths and weaknesses (Eng et al., 2019; Salmen et al., 2018; Wang et al., 2018). When choosing the protocol for one's experimental question, one should consider the spatial resolution, the number of genes studied, the sensitivity, and the throughput. Besides, it is also possible to analyze physical interactions between cells together with scRNA-seq in live tissue by using microdissection and mild dissociation (Boisset et al., 2018).

### Perturbation experiments

Another advance is the possibility to perform gain and loss of function studies with the integration of CRISPR-Cas9 genome editing. This technique is especially powerful for lineage tracing in developmental biology studies, and has been applied to reveal unknown lineage connections in the brain and other organs (Alemany et al., 2018; Griffiths et al., 2018; Raj et al., 2018) and to discover molecular drivers for differentiation (Genga et al., 2019). CRISPR-based screening is also available commercially through 10x Genomics.

## Clinical applications: Stratification of molecular pathology

Due to its strength in analysing molecular properties of single-cells in heterogeneous tissue with high dimensionality and throughput, scRNA-seq has proven to be beneficial in studying the molecular pathology of various disorders. For example, in a mouse model of Alzheimer's disease, scRNA-seq has revealed that different microglial states exist (Keren-Shaul et al., 2017). snRNA-seq has opened a whole new toolbox for the analysis of human pathological processes at the molecular level, including neurological disorders (Habib et al., 2016). For instance, in human Alzheimer patient brain samples, differential gene expression was found in various sub-clusters of excitatory, inhibitory, and glial cells (Mathys et al., 2019). Cellular pathology of multiple sclerosis has also recently been investigated with snRNA-seq revealing pathological changes to specific subgroups of neurons and glial cells showing, for example, selective vulnerability of upper cortical layer excitatory neurons (Jakel et al., 2019; Schirmer et al., 2019). snRNA-seq of autism spectrum disorder samples has similarly revealed changes in upper layer excitatory neurons as well as microglial cells (Velmeshev et al., 2019). The unbiased analysis of all cell types thus reveals specific contributions of cell types that are often overlooked such as glial or senescent cells, but play an important role in disease (Baker and Petersen, 2018). These studies highlight the importance of stratification – different subtypes of cells are differentially involved in disease, and this understanding will allow identifying targets for drug development in the future.

The application of scRNA-seq to clinical research questions will have a significant impact on human health and society. On the European level, the vision of using and further developing single-cell methods has led to the launch of the LifeTime Initiative (lifetime-fetflagship.eu), which has as a mission to "Revolutionize healthcare by tracking, understanding, and treating human cells during diseases".

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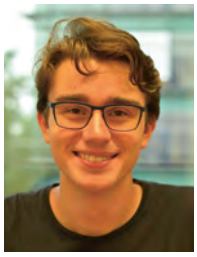
# Bionotes

**Dr. Simone Mayer**
Eberhard Karls University Tübingen
Hertie Institute for Clinical Brain Research
Otfried-Müller-Str. 27
72076 Tübingen, Germany
+49 7071 29-88870
**e-mail: si.mayer@uni-tuebingen.de**
https://orcid.org/0000-0002-6381-2474
https://www.hih-tuebingen.de/de/forschung/unabhaengige-forschungs-gruppen/molekulare-hirnentwicklung/

Dr. Simone Mayer is heading the research group "Molecular Brain Development" at the Hertie Institute for Clinical Brain Research at Tübingen University. During her postdoctoral research at the University of California, San Francisco she has developed a new method of multimodal single-cell analysis and has become fascinated with the possibilities to understand brain development at an unprecedented resolution when integrating single-cell transcriptomics with functional analyses.

**Dr. Shokoufeh Khakipoor**
Eberhard Karls University Tübingen
Hertie Institute for Clinical Brain Research
Otfried-Müller-Str. 27
72076 Tübingen, Germany
**e-mail: shokoufeh.khakipoor@uni-tuebingen.de**

Dr. Shokoufeh Khakipoor is a postdoc in Dr. Simone Mayer's lab at the Hertie Institute for Clinical Brain Research. During her Ph.D. at the University of Freiburg, she has studied how growth factors influence H+ homeostasis in mature neural cells. Now she is enthusiastic to apply her insights from intercellular signalling to the developing brain.



**Maxim A. Drömer**
Eberhard Karls University Tübingen
Hertie Institute for Clinical Brain Research
Otfried-Müller-Str. 27
72076 Tübingen, Germany
**e-mail: maxim.droemer@student.uni-tuebingen.de**

Maxim A. Drömer is a bachelor student in biochemistry and mathematics at Tübingen University and an intern at Hertie Institute for Clinical Brain Research. He is especially interested in understanding functional aspects of neuroscience on the molecular level and therefore prefers an interdisciplinary approach which makes use of molecular biology combined with analysis methods from data science.

**Daniel A. Cozetto**
Eberhard Karls University Tübingen
Hertie Institute for Clinical Brain Research
Otfried-Müller-Str. 27
72076 Tübingen, Germany
**e-mail: dan.cozetto@gmail.com**

Daniel A. Cozetto is a bachelor student in Biotechnology and Bioprocess Engineering at São Paulo State University and intern at Hertie Institute for Clinical Brain Research. Very curious about neuroscience and the molecular identity of the brain, he is interested in understanding the molecular mechanisms that lead to the complex structure of the brain and the development of neurodegenerative diseases.

**Review Article**

Ferdinand Hucho*

# Personal View – The Evolution of Neurochemistry

## Two questions – one answer

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**Abstract:** This esssay is a personal account of the evolution of Neurochemistry in the past century. It describes in parallel the authors way from chemistry to biochemistry and finally to Neurochemistry and the progress of a most exciting chapter of the Life Sciences. It covers the successful time period of reductionist research (by no means comprehensively), which lay the ground for the recent and future systems approach. This development promises answers to fundamental questions of our existence as human beings.

**Keywords:** Chemistry; Biochemistry; Life Science; Neurochemistry

**Zusammenfassung:** Dieser Essay ist ein persönlicher Bericht über die Entwicklung der Neurochemie im vergangenen Jahrhundert. Er beschreibt parallel den Werdegang des Autors vom Chemiker zum Biochemiker und schließlich zum Neurochemiker, und den Fortschritt eines der aufregendsten Kapitel der Lebenswissenschaften. Er behandelt den erfolgreichen reduktionistischen Forschungsansatz (keineswegs umfassend oder lückenlos!), der Grundlage für den systembiologischen Ansatz unserer Tage und der absehbaren Zukunft ist. Diese Entwicklung verspricht Antworten auf fundamentale Fragen unserer Existenz als menschliche Wesen.

**Schlüsselwörter:** Chemie, Biochemie, Lebenswissenschaften, Neurochemie

Neurochemistry is a branch of Biochemistry. Biochemistry in turn originates from Chemistry and Physiology. The latter branched off from Medicine. As a whole this sequence describes in brief the reductionist pathway of life science research in the time span from the late 19th century up to our times. Reductionism was hoped to solve two of the most fundamental riddles which were central to human thinking since antiquity: The world, believed to be composed of ‚mind and matter', poses the question: What is life? The neurochemist goes one step further and asks: what is mind (conciousness, cognition, free will)? The physiologist Emil du Bois-Reymond (1818–1896) included these questions in his ‚seven riddles' (*Finkelstein 2013*) and summarized his answer in 1880 in his famous "*ignoramus et ignorabimus" ("*we don't know and we never will know"*)*. Never say 'never', because this could be the end of human curiosity and research, preventing discoveries including new methods of investigation.

In the 20th century the question *What is life* was most vividly posed by physicists like the Nobel laureates Erwin Schrödinger (*Schrödinger 1944; Fischer ed., 1987*) and Max Delbrück (*Delbrück 1986*). Why physicists? In times of Quantum Physics they suspected a novel matter/mind dualism in living matter similar to the wave/particle dualism of light (Delbrück) or they were waiting for the discovery of still unknown physical laws (Schrödinger). Neither proved to be right.

I found among my notes of a biochemistry lecture presented by Kurt Wallenfels, my teacher and PhD supervisor at the University of Freiburg/Brsg. a quotation by Linus Pauling (1962): "*Life is a property between molecules and not a property of any molecule*". In other words: There is not a single molecule (or at that a group of molecules) defining life. Rather life is a system of interacting molecules which makes matter live. Similarly, there is no *vis vitalis* (a "living force", still postulated by some in the first half of the 20$^{th}$ century; see also the last significant dualist treatise: (*Popper and Eccles, 1977*). Rather life is a special state of the known existing forces, – it is a set of physical parameters embedded in the laws of physics, especially of thermodynamics, which define the living state. The 2$^{nd}$ Law of Thermodynamics postulates an increase of entropy of a system for any exothermic process. Life is a highly unlikely, extremely ordered state of matter, a state of reduced (negative) entropy (Schrödinger,1944). This state can be maintained only as an open system far away from equilib-

***Corresponding author: Ferdinand Hucho**, Institut für Chemie und Biochemie, Freie Universität Berlin, Thielallee 63, 14195 Berlin, Tel. +49 30 3248693, e-mail hucho@chemie.fu-berlin.de

rium (for *non-equilibrium thermodynamics see (Prigogine and Stengers, 1981,)*. Today we would say: This open system extends to the environment of the living organism, and by that includes signal processing and epigenetics. If all processes, metabolic reactions, transport phenomena, information exchange, etc. in living matter like cells and organisms reach equilibrium it means the matter is dead.

So thermodynamics come close to a convincing definition of life and death. We have to admit that this definition leaves many questions unanswered. Our textbooks of biochemistry list in their opening chapters many properties of living matter: metabolism, identical self replication etc. But none subscribes to dualism, none even postulates a special *"mind stuff"*, as the philosopher/neuroscientist Daniel Dennett names it ironically (*Dennett 1991*). The answer to the two questions, the topic of this essay must be found within the laws of physics and chemistry. No serious scientist disagrees.

Given the complexity and the seemingly unsolvability of the problem, it is not surprising that the interest of many researchers faded away and the still unanswered question "What is Life" was set aside for the time being. Molecular Medicine seemed more urgent and rewarding. Recently we observe a certain resurgence of the fundamental question in connection with the growth of a new branch of molecular biology with the rather diffuse denomination 'Synthetic Biology' (*Köchy und Hümpel, eds., 2012)*. Molecular biologists in this field construct among others living matter from organic ('dead') building blocks. They tinker with genomes and genes and try a top down approach asking how few genes are necessary and sufficient to maintain life. If this will be successful, will it answer our question?

## How to become a Biochemist

'*What is Life*' is not the main topic of this essay. Here I would like to ponder over the development of Biochemistry into Molecular Biology and Cell Biology and to one of its most exciting, though mysterious fields: Neurochemistry. This includes the second "*ignoramus, ignorabimus?"*, the most fascinating fact that there is matter in this universe which is not only alive but is conscious and able to think. As was mentioned above, biochemistry has its roots in medical physiology and chemistry of the beginning of the 20$^{th}$ century. I follow this evolution from the viewpoint of a biochemist who started out as a chemist at a time when biochemistry curricula at German universities were still rare. Two impulses started this evolution: One came from basic science asking fundamental questions like the two questions posed in the introductory paragraph above. The other was triggered by the urgent need to get a better understanding and treatment of the many devastating human diseases. I describe this evolutionary pathway following the pathway of the scientific life of a typical biochemist:

Up to the sixties of last century there was only one curriculum of biochemistry offered by a German university, established by Günther Weitzel at the university of Tübingen and started in 1962.

Outside Tübingen therefore one possible way to become a 'biochemist' was to study chemistry (an awfully lengthy and tedious curriculum) and finish this with an experimental diploma work and a subsequent PhD thesis under the supervision of an 'Organic Chemist' interested in the chemistry of life. My choice in Freiburg was Kurt Wallenfels who together with his group synthesized among others homo- and heterocyclic aromatic compounds with strained π-electron systems. This topic is not too far away from electron transfer molecules used by most aerobic organisms in a variety of coenzymes. The Wallenfels group developed more and more interest in biocatalysts (enzyme proteins with and without coenzymes. Of course nothing was heard of RNA- or DNA enzymes at this time).

For the young chemist this offered an attractive entry door from dead chemicals to the chemistry of life: catalysis is an important topic in chemistry and biophysics. The same laws executed with different means and mechanisms, this was enzymology! Enzyme kinetics analyzed with appropriate assays was quite a challenge, promising insight into the structure and function of biocatalysts. Biocatalysts on the other hand are essential for metabolism. One prime difference compared to non-bio catalysts makes enzymes even more interesting: they are flexible; they are able to adjust their efficiency to the needs of an organism. Enzyme regulation is another most important research topic of enzymology. But at the beginning of all biochemical research in 'pre-cloning times' was purification. "*First purify than think! Don't waste pure thinking time on dirty enzymes*" was a statement by an unknown biochemist pinned to the door of my lab. Wisdom like this set the stage for another development essential for the evolution of biochemistry: One could write a history of biochemistry as a history of methods and machinery. Centrifugation, electrophoresis chromatography developed their specific applications in preparative biochemistry. On the structural side progress in protein and DNA/RNA sequencing, X-ray crystallography, mass spectrometry, electron microscopy and the tremendous variety of light microscopic techniques secured advances, just to name few.

**To sum up what I as a biochemist see in retrospect:** *Biochemistry came a long way, originating from physiology. One could say simplistically: it dealt with organs and organisms, i. e. with systems, proceeded to reduced cellular entities and molecules. It returned to molecular systems and moved on to Systems Biology as part of Life Science in our times. The most complex and challenging* ***system*** *known so far is the thinking matter of mind. Let me go on in my description of my personal way from chemistry to Neuroscience.*

## From Lifescience to Neuroscience: The reductionist approach

With regret we see that more and more specialist fields develop in science. On the other hand definitions of those specialties become more difficult and less useful: what is biochemistry? It used to be the chemistry of life. Not knowing what life really is this definition does not make much sense. Some colleagues in the field prefer to call their field molecular biology. This implies that we reduce our focus to molecules rather than cells, organs and organisms. And today the term *Life-science* makes all previous definitions oblique and reunifies scientist from so diverse fields as informatics, ultra structure research, immunology, development, molecular genetics, and many others. It enables specialists to enter new fields and allows them to join teams and cooperations in their effort to add partial answers to our persisting and unanswered questions. As we have seen, by this re-definition the biochemist could move in the middle of the previous century from chemistry, via catalysis and enzymology to metabolic regulation and finally to – Neurochemistry. This latter step needs explanation: what made me, the chemist, a neurochemist?

The obvious answer could be: The obligatory structure of the academic career in Germany of that time: To grow up to an independent researcher required a 'Habilitation'. This was a major step, which after completion allowed to ask oneself: what now? Shall I continue as before or shall I grasp the opportunity to channel my curiosity to an entirely new field? In the early seventies of last century James Watson at Cold Spring Harbor/New York initiated courses aiming at young scientists from various fields who like me were looking for exciting new challenges. This was a wonderful opportunity: three immensely intensive course weeks at a world center of research with great teachers, a Nobel laureate or somebody of similar caliber flown in every other day, W. M. (Max) Cowan slicing three human brains, explaining the overall architecture of the CNS and its development, Thorsten Wiesel elaborating the visual system and its columnar structure, – a constant flow of information from 11.00 a. m. to midnight, 'brain food' for a scientist's life span.

These were the heydays of reductionist Neuroscience. Neuroscience had gone molecular decades before, exemplified by the cholinergic system, my central field of research over the decades 1973–2005: In 1929 Otto Löwi discovered the 'Vagusstoff', identified by Sir Henry Dale as *acetyl choline* shortly thereafter (Nobel prize in Physiology or Medicine in 1936). Sir John Eccles (Nobel Prize in 1963), Sir Bernhard Katz (Nobel Prize 1970), Bert Sakmann and Erwin Neher (Nobel Prize 1991) among others opened the door to our present-day picture of *'chemical neurotransmission'*. The latter three names are linked to the most important development of electrophysiology in the twentieth century, proceeding from wholesale measurements of membrane potentials of excitable cells to single channel currents, i. e. to the molecular events underlying nerve impulses. The *cholinergic system* became my playground starting at Cold Spring Harbor in 1973. After these exciting (and exhausting!) weeks organized by John Nicholls (Neurophysiologist at the Biocenter of the Basel University/ Switzerland) and his team I went to the laboratory of Jean-Pierre Changeux at the Institute Pasteur in Paris to apply experimentally what I had learned just in theory: I learned to purify (remember: "first purify then think…") the *Nicotinic Acetylcholine Receptor,* a protein which Changeux had identified as an entity different from the acetylcholinesterase, the enzyme catalyzing the removal of the '*Vagusstoff,'* the neurotransmitter acetylcholine, from cholinergic synapses. I solved the quaternary structure of the receptor from the electric tissue of the electric eel *Electrophorus electricus*. Work on a protein in the stimulating atmosphere of Changeux' laboratory, the discoverer of allosterism as a fundamental mechanism of regulation of oligomeric biocatalysts, gave a good start. I was able to contribute to an entirely new field, on the basis of what I had learned as a chemist/biochemist before.

Meanwhile Neurochemistry became molecular throughout: Shosaku Numa was first to clone and sequence a cDNA coding for the α-subunit of the nicotinic acetylcholine receptor from the electric ray Torpedo spc. (1982), with many others to follow. Ion channels, transporters, components of what became the new field of signal transduction and intracellular signaling emerged from various experimental approaches and were characterized on the molecular level. More and more 3D structures were elucidated with atomic resolution.

**In brief: What is reductionism?** The final aim of neuroscience is to understand the (human) brain, presumably

the only substance in the universe able to think, to be conscious, and to exert a free will (of course the human brain shares these capacities with other animals to varying degrees). One method to understand it is to analyze its functional elements. Among these elements ion channels, receptors, transporters, membranes, synapses play important roles. Reductionists hope to reconstruct complex functions of nerve systems from their functional components. Of course this implies already the limits of this method: The whole (the system) is always more than just the sum of its parts. A word is more than the addition of letters. Even more so are complex texts, composed of words, sentences, language. A meaningful text requires more than letters and words: Without grammar and semantics there is no useful text in any language.

Fortunately, the functional molecular components in the nervous systems throughout the animal kingdom follow similar principles: Therefore reductionism on the organismic scale was (and still is) useful. To understand signaling of nervous systems does not require investigation of the human brain. Nerve impulse propagation was elucidated with squid giant axons, simple nervous systems underlying behavior were successfully investigated with invertebrates like the leech and the sea snail aplysia, just to mention two examples. This type or reductionism is called *methodological reductionism*. Philosophers (*Wuketits 1989*) add to it a strategy which is called *"Episthemiological Reductionism"* which as a matter of fact is an expansion which helps to discover more comprehensive principles. A third definition of reductionism, called "*Ontological Reductionism",* has to be discarded at least for the Life Sciences because it postulates to reduce a complex phenomenon to its 'smallest parts'. Methodological Reductionism can be exemplified by molecular genetics: *"What is true for Escherichia coli is true for the elephant",* this is a famous definition of the reductionist belief by the micro biologist Jacques Monod (Nobel prize 1965). It is still valid today with respect e. g. to the DNA structure, the genetic code and some features of gene expression, but the limitations of its meaning for the genetics (incl. epigenetics) of 'higher' organism is obvious. First of all, the genome is a *system,* a network of *about* 20.000 genes (in humans) the expression of which is regulated manifold, *via* expression factors, gene products and signaling cascades, just to name a few regulators. The expression pattern, not the genes as such make the species and the individual. It is trivial to state: both the reduction of genetics to its molecular elements *and* the sum of the molecular interactions in the system must be elucidated to understand molecular genetics. It is not *either* reductionism *or* systems biology; both are fundamental to understanding complex phenomena as life and mind.

In a thoughtful essay in this journal Martin Heisenberg covers this subject, albeit limited to animal *(Drosophila)* life (*Heisenberg, M. 2018)*. In this essay Heisenberg narrows the gap between Mind and Matter: Mind (german *Geist, Seele*) is an important result of evolution which increases the fitness of an organism for survival and reproduction. Heisenberg in his essay calls this beneficial property *behavior* and he observes in the insect's behavior "indirect, mental" elements as for example'intentionality', 'attention', 'formation of hypotheses', 'emotions', 'motivation' 'sociality' etc. All living organisms 'behave' (if we accept the definition that behavior is the interaction of an individual organism with others and with its environment). To improve and sustain behavior signal reception and processing, signaling cascades and finally nerves and neuronal systems evolved. All living organisms accordingly possess mind (again: german Geist, Seele). Note that this definition does not include consciousness, free will! It describes an increase of complexity, at the end of which stands the most complex matter known, the human brain. Philosophers coined the term *emergence:* the conscious mind is emerging from dead matter *via* life matter and unconscious nervous tissues. Consciousness is located in the cortex of the brain; most of the human brain is unconscious. But what is the difference in structure and functional mechanism of the unconscious and the conscious? This is the other 'ignoramus', the fascinating property of thinking matter: The human brain is not only alive, it can dream (passively), actively plan, intend, want, – but how? *ignorabimus?*

## Neuropharmacology

The prime beneficiary of reductionist neuroscience was – and still is – molecular pharmacology. Molecules involved in nerve impulse propagation and transmission are targets of drugs and therapeutic treatments. This was one of the justifications of *receptorology*: Neurotransmitter receptors are key protein molecules pivotal in signal transmission and processing. They were postulated to exist by J.N. Langley (1878) long before being isolated in the test tube. Langley coined the term 'receptive substance' in 1905. Receptors were first identified and isolated in the seventies of last century. Up to that time they were more or less plausible concepts, no molecular realities. After a time of tedious protein identification and purification, the field exploded with the advent of cloning technologies.

**Diversity through multiplicty:** Classical neurochemistry had discovered a rather limited number of neurotransmitters so far, small molecules transmitting the electrical signal from the presynaptic side of a synapse over the synaptic cleft to the postsynaptic side where they trigger an electrical signal again (or a signaling cascade of molecules within the target cell, respectively). The paucity of neurotransmitters seemed to be in contrast to the vast multiplicity of functions in the brain. One would expect that novel properties of many molecules interacting as 'systems' emerge from complexity. How can this happen if only one dozen or two transmitters and their respective receptors are available? The solution (at least in part) was found in the multiplicity of receptors: Most of the transmitter receptors are hetero oligomeric proteins. They occur in various combinations of similar but distinctively different polypeptide chains. The prototype inhibitory $GABA_A$ Receptor e. g. is a pentamer composed of four (resp. 5) types of polypeptide chain coming in a number of variants. Theoretically one can easily construct more than thousand different hetero pentamers with them. Of course not all of them occur *in vivo*. But it opens not only the possibility of quite a variety of tissue specific expression and function of the various subunits and by that of different receptors. It also offers a multitude of small molecule-binding sites, which are often located at the interfaces between subunits. The recently published high resolution 3D structure of a $GABA_A$ Receptor elucidated by electron cryo-microscopy with the receptor protein heterologously expressed in HEK cells and functionally reconstituted in lipid nanodiscs is proof of this principle. This receptor is an inhibitory ligand gated chloride channel. Its specificity for benzodiazepine binding requires the presence of the ß2 subunit. The transmitter GABA binds to the αß interface while benzodiazepines bind (non competitively) to the αγ interface, the high resolution images of which give optimal information for rational drug design. The molecular basis of receptor multiplicity and functional diversity of drug targets is hoped to lead to more specific drugs with fewer side effects. But on the other hand it introduces a level of complexity which makes research more challenging. This may be a reason why we observe that many of the major drug companies gave up CNS research alltogether. They are not willing to risk the time and money it takes to bring a drug candidate from the "bench to the bedside". This observation is in favor of investing more into government supported basic research at universities and public institutions.

***Toxins as tools in Neurochemistry:*** The best molecular neuropharmacologist is still 'Mother Nature': Many animals use neurotoxins as a means for defense and for hunting prey. Most of them interact in minute amounts with maximal specificity with key functional sites in the nervous system of enemies resp. prey. By this they supply science with efficient tools to identify and analyse such sites: Snake venom toxins *(e.g. α-Bungarotoxin)*, Black widow spider toxins *(α-Latrotoxin)*, Scorpion toxins, Tetrodotoxin, but also sea anemone toxins and toxins from plants and bacteria are a few examples of the long list of this potent tool kit which served basic science to isolate receptors, ion channels, synaptic components, and other signaling molecules.

This leads me to a more political aspect of my activity in the years starting in the early eighties of last century: my cooperations and friendship with colleagues in the former Soviet Union. Traditionally life scientists were oriented westwards. Accepting a position in Berlin (then called "*Westberlin*") in 1979 made me turn around and look for links to the East, hoping to pierce tiny holes into the *Iron Curtain*. Of course official support of these activities on the Russian side was stimulated by non-scientific afterthoughts circling around the deadly neurotoxins (Leitenberg and Zilinskas 2012), but the positive 'side effect' was a vivid exchange of contacts, symposia and summer schools. These contacts resulted in fruitful cooperations with the best Russian neurochemists, culminating in a 1 1/2 year visit in my laboratory by Victor Tsetlin, who was awarded a Humboldt professorship.

## Trends of the past, present, and future

Neurochemistry came a long way, from medicine, chemistry, biochemistry, to its present day state. In other words: it proceeded from biological *systems*, through *reductionism* focussing on simple models and functional components, and it arrived again at *systems* biology. The basic questions, the starting point of this essay, remain unanswered. The common answer to both questions is: *ignoramus*, but they will be answered, if not by this or the next generation by a generation to come: with new ideas and new methods.

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# Bionotes

**Prof. a. D. Dr. rer. Nat. Ferdinand Hucho**
Institut für Chemie und Biochemie
Freie Universität Berlin
Thielallee 63
14195 Berlin
Tel. +49 30 3248693
**e-mail: hucho@chemie.fu-berlin.de**

Ferdinand Hucho, born 1939 in Berlin, studied Chemistry in Freiburg/Breisgau. He obtained his PhD in1968 with work on the catalytic mechanism of a bacterial enzyme under the supervision of Kurt Wallenfels, He did his first postdoc 1969–70 with Lester Reed at the University of Texas at Austin working on the regulation of multi enzyme complexes. His second postdoc he did in the lab of Horst Sund at the University of Konstanz/Germany. There he got his Habilitation in 1973 with work on the regulation of pyruvate dehydrogenase by a protein kinase. Short visits to Cold Spring Harbor and to Paris allowed him to switch to neurochemistry. In 1979 he became a professor (with tenure) at the University of Konstanz. The same year he moved to the Freie Universität Berlin. His main field of interest were the structure and functional mechanism of neurotransmitter receptors. In 1997 he was elected as a member to the Berlin-Brandenburg Academy of Sciences and Humanities. There he initiated a long term monitoring project observing the development of Gene Technology in Germany.

**Presentation of Scientific Institutions**

Christian Schmahl and Sylvia Cackowski*

# Research Training Group (RTG) / Graduiertenkolleg (GRK) 2350

## "Impact of Adverse Childhood Experiences on Psychosocial and Somatic Conditions Across the Lifespan"

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In April 2018, the Research Training Group (RTG) 2350 "Impact of Adverse Childhood Experiences on Psychosocial and Somatic Conditions Across the Lifespan" which is funded by the German Research Foundation (DFG) started. The RTG 2350 investigates psychosocial, neurobiological, and somatic sequelae of adverse childhood experiences (ACE) in 15 different projects. It is embedded in the central lines of research at the Central Institute of Mental Health (CIMH) and the Medical Faculty Heidelberg (MFH), with two already existing BMBF funded networks on trauma-related disorders and existing patient cohorts, and based on long-lasting experience with doctoral training programs. ACE such as sexual and physical abuse or neglect are frequent in childhood and constitute a massive stressor with long-lasting consequences for mental and physical health. Despite their obvious relatedness, neither the causal relation nor the mechanisms involved are clear. On the one hand, traumatic experiences are diverse, differing in type, timing, and intensity with social support and other protective factors contributing to this. On the other hand, ACE-related manifestations range from psychosocial to somatic problems such as heightened stress sensitivity, emotional disturbances, interpersonal problems, depression, substance dependence, chronic pain, or inflammatory and metabolic diseases.

Therefore, the central aims of the RTG are (1) Investigation of the role of type, timing and intensity of ACE and protective factors in the emergence of ACE-related disorders; (2) Elucidation of the psychosocial, neurobiological and epigenetic mechanisms underlying ACE-related psychiatric and somatic disorders; (3) Development of novel psychosocial and pharmacological treatment possibilities as well as public health programs for ACE-related conditions.

To cover the interdisciplinary research area, namely the consequences of adverse childhood experiences (ACE) on psychosocial and somatic conditions broadly and profoundly and reach all aims of the RTG, a representative selection of research topics across the psychological and biological medical domains was made and senior as well junior PIs with a wide spectrum of expertise are part of the RTG. The individual projects span a broad range from epidemiological and clinical research to experimental studies in animals and humans including genetics, neuroimaging and ecological momentary assessment. A special feature of the RTG is the integration of psychological, psychiatric and somatic topics, which is mirrored by close working together of PhD and MD students. As an example, one of the projects investigates the impact of abuse and neglect in childhood on psychological wellbeing during pregnancy and childbirth. Besides, biological parameters such as pain sensitivity and hormonal level are assessed and will be used in combination with the psychological data to develop better care for traumatized pregnant women.

After passing an application procedure and assessment center, 21 international postgraduates with a background in medicine, psychology, biology, and related natural sciences were selected as RTG members and started their work on doctoral theses. Additional to their experimental studies the doctoral students participate at the structured concept for qualification and supervision. The RTG 2350 trains doctoral researchers to provide a substantial basis for a potential international scientific career. Scientific development is facilitated by the participation in regular events like research presentations and scientific exchange at journal clubs, progress reports and at international conferences, symposia, and a master class with international experts. Also, the doctoral researchers

***Corresponding author: Dr. Sylvia Cackowski**, Department of Psychosomatic Medicine and Psychotherapy, Central Institute of Mental Health, J5, D-68159 Mannheim, Germany; Phone number: (+49-)621-1703-4431; Fax: (+49-)621-1703-4405; e-mail: sylvia.cackowski@zi-mannheim.de

have the possibility to gain practical experience during internships in internationally leading RTG partner research groups. Beside intensive training in scientific excellence, providing key knowledge, hard and soft skills the doctoral students receive additional support through mentoring and coaching to promote personal development.

Taken together, the RTG 2350 aims to support self-responsible, personal, and professional development of young researchers and to provide them with skills and competencies for their further careers in either academia or other areas.

The understanding of the complex ACE-related characteristics and mechanisms is relevant for mental and somatic disorders. Identifying and validating psychosocial and somatic risk factors and diagnostic markers shall result in the development of innovative somatic and psychological treatment options for patients suffering from ACE-related disorders.

Website: https://www.grk2350.de/

**Presentation of Scientific Institutions**

Friederike Langhauser und Christoph Kleinschnitz*

# Forschergruppe (FOR 2879) ImmunoStroke: Von der Immunzelle zur Schlaganfallregeneration

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Die Deutsche Forschungsgemeinschaft (DFG) richtet eine neue Forschungsgruppe zum Schlaganfall ein. Der Forschungsverbund mit dem Namen „ImmunoStroke: from immune cells to stroke recovery“ (ImmunoStroke: Von der Immunzelle zur Schlaganfallregeneration) ist ein Gemeinschaftsprojekt der Universitäten Essen, Hamburg, München und Münster und wird mit rund 4,5 Mio. Euro in den ersten 3 Jahren gefördert. Ziel der Wissenschaftlerinnen und Wissenschaftler ist es, die Rolle des Immunsystems in der Regenerationsphase nach einem Schlaganfall zu untersuchen und neue Behandlungsmöglichkeiten zu entwickeln. Koordinatoren des Verbundes sind Christoph Kleinschnitz aus Essen, Tim Magnus aus Hamburg und Arthur Liesz aus München.

Der Schlaganfall ist die Hauptursache für Langzeitbehinderungen und die dritthäufigste Todesursache in Industrieländern. In Deutschland liegt die jährliche Schlaganfallinzidenz bei über 250.000. Das Lebenszeitrisiko bei einem Schlaganfall liegt zwischen 8 % und 10 % und steigt aufgrund demografischer Veränderungen weiter an. Gegenwärtige Behandlungen für Schlaganfälle sind begrenzt, und präklinische experimentelle Ergebnisse scheitern häufig in klinischen Studien. Daher sind dringend neue Wege der Grundlagenforschung mit hohem Übersetzungspotenzial erforderlich, um wirksame therapeutische Strategien zu entwickeln. Die neuroinflammatorische Reaktion nach einer ischämischen Hirnverletzung ist als Schlüsselpathomechanismus beim Schlaganfall gut etabliert. Während neuroinflammatorische Mechanismen für die akute Phase nach einer ischämischen Hirnverletzung sehr detailliert beschrieben wurden (Gelderblom et al., 2012; Kleinschnitz et al., 2010; Kleinschnitz et al., 2013; Liesz et al., 2009), sind die Mechanismen der Gehirn-Immun-Interaktion während der chronischen Erholungsphase sowie die Folgen immunmodulatorischer Interventionen für die Erholung nach einem Schlaganfall kaum bekannt. In ersten Experimenten konnten die Wissenschaftlerinnen und Wissenschaftler mithilfe verschiedener Modelle zeigen, dass insbesondere T Zellen und Mikroglia und deren Interaktion mit Neuronen eine wichtige Bedeutung für das langfristige Schlaganfalloutcome haben.

Die Teilprojekte A1-A4 der Forschergruppe basieren auf der Beobachtung, dass ein Schlaganfall zu einer anhaltenden Mikroglia-Aktivierung führt. Projekt A1 wird die Wirkung von sogenannten „Gefahrensignalen“ (danger-associated molecular patterns, DAMPs) als Aktivatoren der lokalen Immunantwort beim Schlaganfall untersuchen (siehe Abbildung 1). Dabei kommen neuartige Nanobodies gegen Gefahrensignalrezeptoren, wie z. B. den P2X7 Kanal zum Einsatz. Die Aktivierung des P2X7 Kanals führt zur Aktivierung von Inflammasomen, die in Projekt A2 untersucht werden. Neben der Analyse von IL-1β als dem klassischen proinflammatorischen Zytokin, das durch Inflammasomaktivierung freigesetzt wird, wird diese Teilprojekt auch die nicht-inflammatorischen Mechanismen des Inflammasoms in der synaptischen Plastizität durch Mechanismen lokal begrenzter Pyroptose untersuchen. Projekt A3 wird den Effekt der chronischen Mikroglia-Aktivierung auf die funktionelle Erholung nach einem Schlaganfall untersuchen. Dazu werden Mikroglia nach dem Schlaganfall entweder in zeitlichen Abständen oder dauerhaft depletiert und die Auswirkungen dieser Mikroglia-Depletion auf die neuronale Netzwerkfunktion, neuronale Plastizität und auf das Verhalten analysiert. Wichtig für die funktionelle Erholung ist auch die Gefäßneubildung in den ischämischen Arealen. Deshalb wird die mikrovaskuläre Integrität in der Phase der Gefäßneubildung nach einem Schlaganfall in Anhängigkeit von Mikroglia und T-Zellen im Projekt A4 untersucht.

***Corresponding author: Prof. Dr. med. Christoph Kleinschnitz, MHBA,** Direktor Klinik für Neurologie, Sprecher FOR 2879, Universitätsklinikum Essen (AöR), Klinik für Neurologie, Hufelandstraße 55, D-45147 Essen, Telefon: +49-201-723-2460, Telefax: +49-201-723-5901, E-Mail: Christoph.Kleinschnitz@uk-essen.de
**Dr. Friederike Langhauser**, Universitätsklinikum Essen (AöR), Klinik für Neurologie, Hufelandstraße 55, D-45147 Essen, E-Mail: Friederike.Langhauser@uk-essen.de

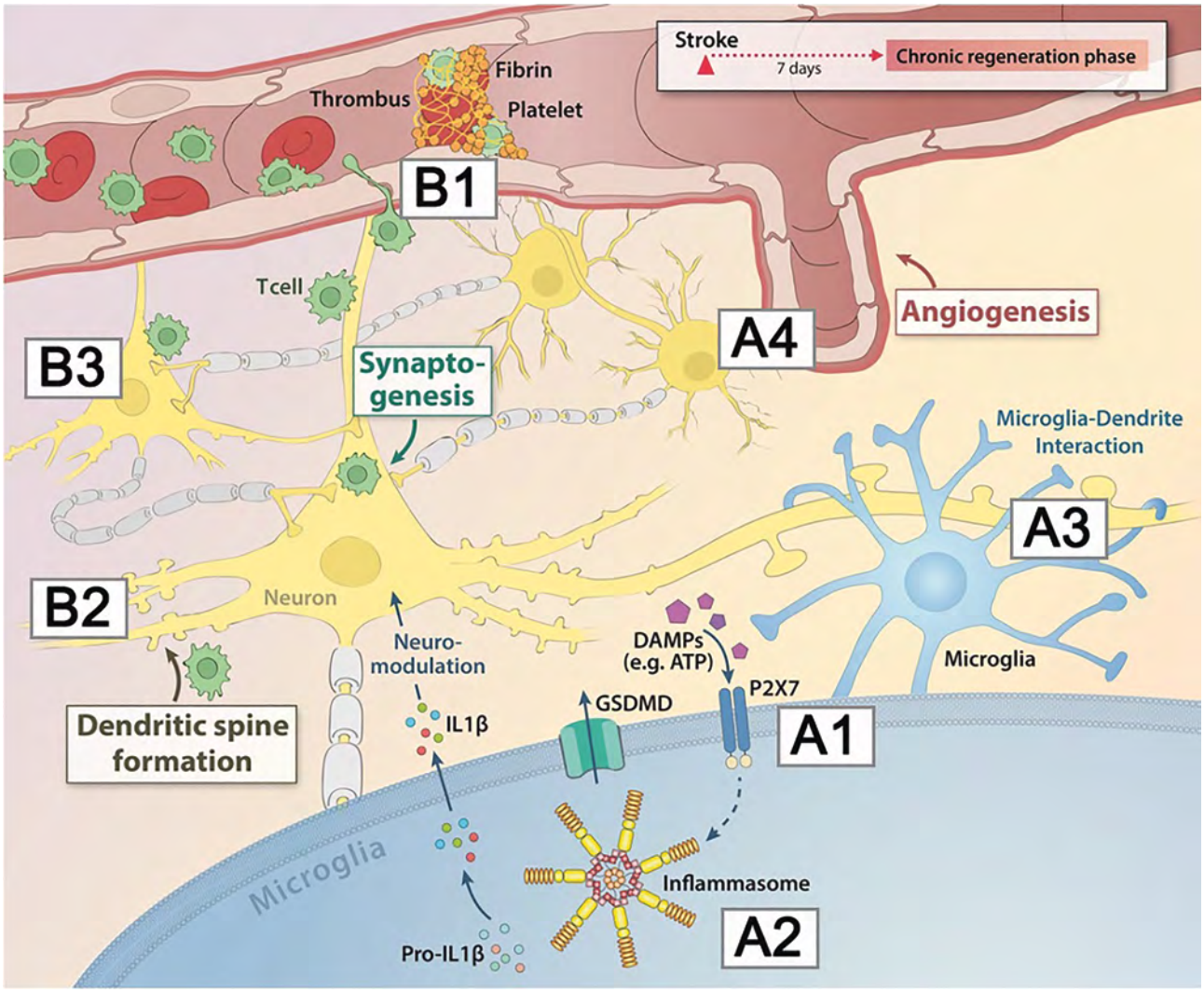


**Abb. 1:** Gezeigt ist die Modulation verschiedener Regenerationsprozesse nach einem Schlaganfall durch T-Zellen und Mikroglia und die thematischen Ansatzpunkte der präklinischen Projekte. T-Zellen und Mikroglia sind die Hauptbestandteile der chronischen neuroinflammatorischen Reaktion nach Schlaganfall. Während Mikrogliazellen auch in der chronischen Phase einen aktivierten Phänotyp beibehalten, werden T-Zellen ständig für das verletzte Gehirn rekrutiert. Sie beeinflussen nicht nur das Überleben und Wachstum von Neuronen und die Ausbildung neuer Synapsen, sondern modulieren auch Zytokinfreisetzung, Angiogenese und intravaskuläre Effekte wie chronische Thromboinflammation.

Die Projekte B1-B3 fokussieren sich auf die Rolle der T Zellen bei der Schlaganfallregeneration. Dabei wird Projekt B1 die Rolle von T-Zellen bei der durch das Kallikrein-Kinin-System vermittelten Thromboinflammation während der Regenerationsphase unter Verwendung spezifischer Knockout-Mäuse und neu entwickelter Inhibitoren messen. Projekt B2 wird den Einfluss einer Trainingstherapie auf das räumliche Verteilungsmuster, auf Genexpressionsprofile und funktionelle Eigenschaften von T-Zellen und deren Effekte auf axonales Wachstum und neuronale Exzitabilität analysieren. Ziel von Projekt B3 ist es, Kandidatengene zu identifizieren und zu charakterisieren, die für schädliche oder schützende neuronale Reaktionen nach einem Schlaganfall verantwortlich sind. Dafür werden Veränderungen der neuronalen Expression nach einem Schlaganfall in Abhängigkeit des proinflammatorischen Zytokins IL-17 und des antiinflammatorischen Zytokins IL-10 analysiert.

Die Forschergruppe setzt aber nicht alleine auf experimentelle Studien. Deshalb gibt es innerhalb des Konsortiums auch zwei humane, translationale Projekte. In Projekt C1 werden die Veränderungen des peripheren Immunsystems im Kontext einer zerebralen Ischämie in Abhängigkeit von der Schlaganfall-Lokalisation, Läsionscharakteristika, dem klinischen Verlauf und dem Auftreten von Komplikationen charakterisiert. Dabei erfolgt

bei Schlaganfallpatienten neben dem initialen MRT eine systematische Kartierung des peripheren Immunsystems, um läsionsspezifische Unterschiede in der Immunsignatur sowie mögliche Frühindikatoren für eine spätere Schlaganfall-assoziierte Immunsuppression zu identifizieren. Außerdem wird untersucht, ob im Rahmen des Schlaganfalls Veränderungen des Immunzell-Metabolismus beobachtet werden können. Das zweite Humanprojekt, C2, wird dieselbe Patientenkohorte wie Projekt C1 untersuchen. Unter Verwendung von neuartigen Mikroglia-PET-Tracern wird die Mikrogliaaktivierung nach humanem Schlaganfall untersucht und die Beziehung zwischen Mikrogliaaktivierung, zirkulierenden Entzündungsmarkern, Infarktentwicklung, sekundärer Neurodegeneration und klinischem Outcome analysiert. Darüber hinaus werden auch in Mäusen Mikroglia-PET Untersuchungen nach Schlaganfall durchgeführt, um einen direkten Vergleich der Mikrogliaaktivierung zwischen Mensch und Maus zu ermöglichen.

Diese Validierung am Menschen ist enorm wichtig, um die translationale Relevanz der experimentellen Befunde richtig einordnen zu können. Möglich wird das erst durch einen breiten interdisziplinären Ansatz, der Expertinnen und Experten aus den Bereichen der Schlaganfallforschung, der Neuroimmunologie, der Neurobiologie und der klinischen Neurologie zusammenbringt. Eine weitere Besonderheit von ImmunoStroke ist ein Zentralprojekt, welches Trainingsworkshops veranstaltet und verbindliche SOPs zur Verfügung stellt, um eine konsequente Vereinheitlichung aller experimentellen Modelle innerhalb des Konsortiums zu gewährleisten. Wichtige Erkenntnisse aus der ersten Förderperiode sollen in präklinischen, randomisierten Multicenterstudien in der zweiten Finanzierungsphase validiert werden.

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## Bionotes

**Prof. Dr. med. Christoph Kleinschnitz, MHBA**
Direktor Klinik für Neurologie
Sprecher FOR 2879
Universitätsklinikum Essen (AöR)
Klinik für Neurologie
Hufelandstraße 55, D-45147 Essen
Telefon: +49-201-723-2460
Telefax: +49-201-723-5901
**E-Mail: Christoph.Kleinschnitz@uk-essen.de**

## Rezension

**Maren Urner:** Schluss mit dem täglichen Weltuntergang – Wie wir uns gegen die digitale Vermüllung unserer Gehirne wehren.

besprochen von **Sophie Seidenbecher**, Aarhus Universitet, Molecular Biology and Genetics, Hoegh-Guldbergsgade 10, 8000 Aarhus, DENMARK; seidenbecher@dandrite.au.dk

https://doi.org/10.1515/nf-2019-0026


Die Neurowissenschaftlerin und *Perspective Daily* Mitbegründerin Maren Urner beschreibt in Ihrem Buch *Schluss mit dem täglichen Weltuntergang- Wie wir uns gegen die digitale Vermüllung unserer Gehirne wehren* eine Negativspirale aus suchtähnlichem Medienkonsumverhalten und einem zum Dramatisieren tendierenden Journalismus, die je nach Disposition entweder beim „stressbedingten Herzinfarkt“ oder einem Keller voll selbstgemachter Marmelade endet („neuer Biedermeier“). Als Ausweg schlägt sie eine Kombination aus Verhaltensänderungen, kritischem Denken und konstruktivem Journalismus vor. Letzteren betreibt sie selbst auf ihrer Webseite *perspective-daily.de*, auf der Wissenschaftler journalistische Beiträge liefern, die neben der thematischen Zustandsbeschreibung auch einen Ausblick auf vorhandene oder denkbare Lösungen geben.

Das Buch umfasst ihre Gedanken und Erkenntnisse rund um diese Themen, inklusive Parforceritt durch Studien und Forschungsergebnisse aus Psychologie und Neurowissenschaft um ihre Thesen zu Fähigkeiten und Funktion unseres Gehirns zu untermauern.

Unter anderem kritisiert die Autorin wiederholt den Fokus der Medien auf Krisen und Katastrophen, der beim Leser allein schon durch die Wortwahl zu negativen Emotionen und Hilflosigkeit im Angesicht des schlechten Zustands der Welt führt. Dass sie in ihrer Darstellung zuweilen selbst ein überaus negatives Bild der Einflüsse schlechter Nachrichten auf unser Gehirn entwirft fällt dadurch umso stärker auf und bedingt die Frage, ob denn dieselben Sprachbilder gerechtfertigt sind solange nur am Ende des Textes ein positiver Ausblick geboten wird.

Als Leser ist man in diesem Buch Betroffener, Angeklagter und Verbündeter, und dies im schnellen Wechsel von einem zum nächsten Unterkapitel. Dadurch bleibt unklar an wen sich das Geschriebene richtet, welches sich am Ehesten als mit Wissenschaftsanekdoten gespickte Werbung für ihr Unternehmen zusammenfassen lässt. Entsprechend bleibt man an so mancher Stelle unbefriedigt zurück, wenngleich auch neugierig auf eine Kostprobe ihres konstruktiven Journalismus.

Dieser erscheint durchaus zeitgemäß und unterstützenswert und die im Buch beschriebene Arbeitsweise der *Perspective Daily* Redaktion wirkt gut durchdacht und positiv idealistisch. Auch ihr Ziel wissenschaftliche Erkenntnisse (zum Guten) in den journalistischen Schreibprozess einfließen zu lassen erscheint überfällig.

Und tatsächlich erweist sich *Perspective Daily* als ansprechend und funktional gestaltetes Onlinemagazin, welches eine mögliche Ergänzung zum aktuellen tagespolitischen Medienkonsum darstellen kann. Es könnte sich lohnen die Entwicklung der Ideen von Maren Urner und ihren Mitstreitern weiterzuverfolgen. Das Buch muss man dafür nicht unbedingt lesen.

***Maren Urner***
***Schluss mit dem täglichen Weltuntergang –***
***Wie wir uns gegen die digitale Vermüllung***
***unserer Gehirne wehren.***
*Droemer, München 2019; 222 S., 16,99 €*
*ISBN-10: 342627776X*
*ISBN-13: 978-3426277768*

## Nachrichten

https://doi.org/10.1515/nf-2019-0032

# Göttinger Jahrestagung 2019

*Eckhard Friauf*

Besonders für das Berliner Büro der NWG bedeutet eine gerade vergangene Göttinger Tagung bereits den bevorstehenden Beginn der nächsten. Zum 13ten Mal ist das nun der Fall. Die Auswertung und Nachbereitung der Göttinger Tagung 2019 gelangt mit dem vorliegenden Bericht zum Abschluss, gleichzeitig erscheint in dieser Neuroforum-Ausgabe der Call for Symposia für die Göttinger Tagung 2021. Erfreulicherweise kann der Bericht viel Positives vermelden. Hoffentlich werden Sie, werte LeserInnen, auch deshalb zur Beteiligung an der nächsten Tagung motiviert. Sie wird vom 24.–27. März 2021 stattfinden; mark your calender!

Dieses Jahr hatte die NWG vom 20.–23. März nach Göttingen eingeladen. Verglichen mit 2017 blieb die Zahl der angemeldeten Teilnehmer annähernd stabil. Dies ist erfreulich, da in der neurowissenschaftlichen Kongresslandschaft eher ein Trend weg von multidisziplinären und hin zu fachspezifischen Meetings zu beobachten ist sowie nach dem FENS Forum 2018 binnen Jahresfrist eine zweite, ähnlich ausgerichtete Neuro-Tagung „vor Ort“ stattgefunden hatte. Auch sonst gab es wenig Abweichungen von der letzten Tagung. Mit Teilnehmern aus 42 Ländern hatte sie internationales Flair, auch wenn 74 % der Teilnehmer aus dem Inland kamen. Der größte Teil der Teilnehmer kam mit 24 % bzw. 23 % aus den Sektionen Zelluläre Neurobiologie und Verhaltensneurowissenschaften (Abbildung 1). Diese beiden Sektionen umfassen 23 % bzw. 12 % der NWG-Mitglieder. Die Sektion Zelluläre Neurobiologie war somit auf der Tagung nahezu optimal repräsentiert. Aus den Sektionen Entwicklungsneurobiologie/Neurogenetik und Neuropharmakologie kamen 5 % bzw. 2 % der Teilnehmer. Diese Sektionen umfassen 7 % bzw. 6 % der NWG-Mitglieder. Die Sektion Neuropharmakologie war somit auf der Tagung 2019 stark unterrepräsentiert. Für mich ergibt sich dadurch für die eine oder andere Sektion die Aufgabe, dem bestehenden Ungleichgewicht entgegenzuwirken.

Die Göttinger Tagung ist nach wie vor ein Meeting für junge Neurowissenschaftler. Dies zeigen die Zahlen in Abbildung 2. Etwa ein weiteres Drittel sind jünger als

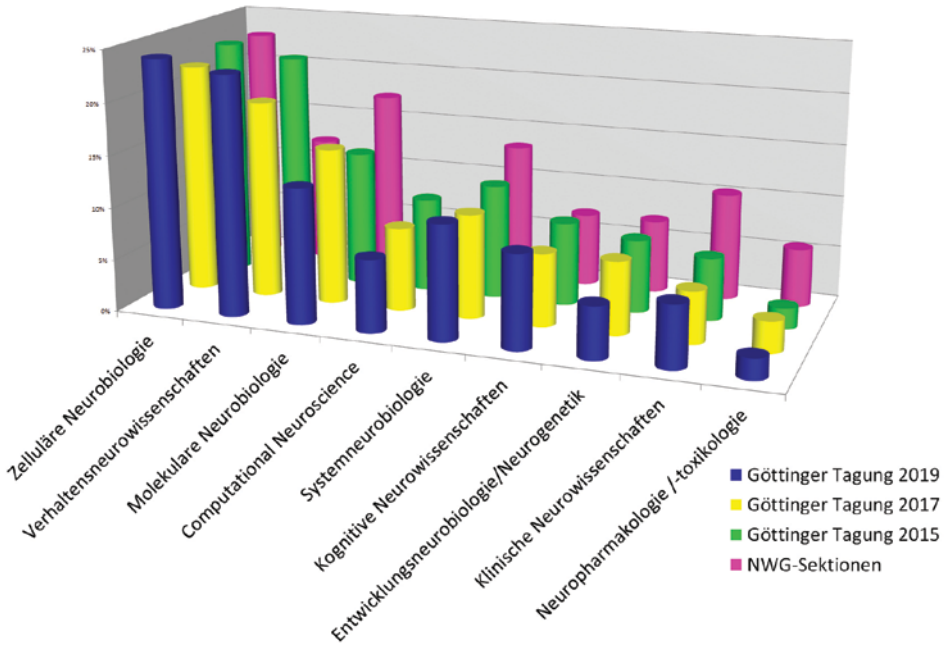


**Abb. 1:** Repräsentanz der neun NWG-Sektionen auf den Göttinger Tagungen 2015 – 2019.

als 40 Jahre. Die Ü50-Generation macht nur ein Sechstel der Teilnehmer aus, hier besteht meines Erachtens Verbesserungspotenzial. Ich wünsche mir, dass mehr arrivierte Wissenschaftler die Tagung durch ihre Anwesenheit bereichern und den Jungen Gelegenheit geben, auf Augenhöhe mit „Big Shots“, die sie sonst nur aus Publikationen kennen, zu kommunizieren.

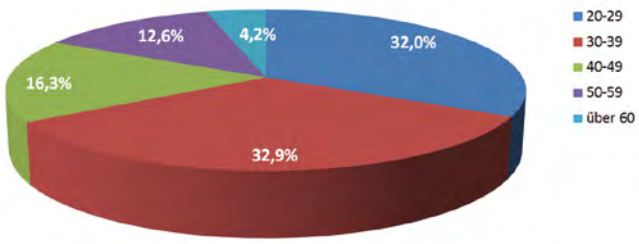


**Abb. 2:** Altersverteilung der Teilnehmer

Dass zwei Drittel der Tagungsteilnehmer jünger als 40 Jahre sind, spiegelt sich auch darin wider, dass sich ebenfalls zwei Drittel als Student oder Postdoc registrierten (Abbildung 3). Mir wäre es recht, wenn der Anteil der Postdocs bei zukünftigen Meetings größer würde. Die NWG kümmert sich in vielerlei Hinsicht um die jungen Kongressteilnehmer. Das Programm sieht viel Zeit für die Poster Sessions vor. Es gibt zwei Vortragslots, die in jedem der 36 Symposien für Studenten (Doktoranden) reserviert sind. Die Teilnehmergebühr für Studierende war mit 75 € äußerst günstig. Kaffeepausen, Wasser und Abendbuffets sind kostenlos. Es gibt hochwertige Gewinne bei der Passport Competition, die Verlosung eines iPads für die Abgabe der Kongressbewertung und, last not least, die Göttinger Neuroparty. All diese Maßnahmen machen offenbar die Göttinger Tagung für ein junges Publikum attraktiv.

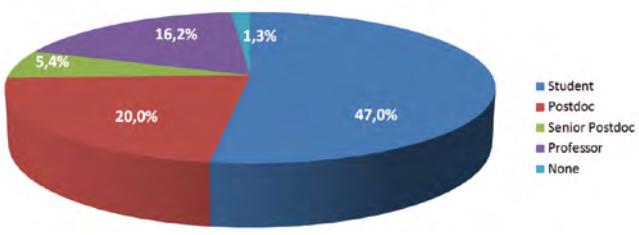


**Abb. 3:** Beruflicher Status der Teilnehmer

Die Bewertung des wissenschaftlichen Teils der Tagung durch die Teilnehmer fasst Abbildung 4 zusammen. Auf der positiven Seite fallen drei Aspekte besonders auf: Die Qualität der Hauptvorträge, die Raumsituation und die Pünktlichkeit. Diese drei Aspekte erhielten >90 % exzellente bis gute Bewertungen. Auf der negativen Seite fällt auf: die Relevanz des Themas für die eigene Arbeit, die Unausgewogenheit zwischen grundlagenorientierten und klinisch ausgerichteten Thematiken und eine zeitliche Überlappung mit anderen Programmpunkten. Diese drei Aspekte wurden von >20 % der Befragten mit schwach bis sehr schlecht bewertet.

Fünf der neun Hauptredner kamen aus dem Ausland, es gab drei Hauptrednerinnen. In den 36 Symposien wurden 207 Vorträge gehalten, 67 davon von Rednern aus dem Ausland, 94 von Frauen. Zwei der Symposien wurden als Breaking-News-Veranstaltung für die Nachwuchswissenschaftler angeboten. In ihnen wurden dieses Jahr erstmals drei Geldpreise für die besten Vorträge vergeben. Auch in den kommenden Meetings wird dies so sein.

Für die zukünftigen Tagungen ist es wünschenswert, dass die Bewerbung der Symposien stärkere Resonanz findet und die Einreichung von Vorschlägen mehr forciert wird. Besonders aus Sonderforschungsbereichen, Schwerpunktprogrammen, Forschergruppen und Graduiertenkollegs erhoffen wir uns spannende und interessante Akzente, zumal damit diese konzertierten Programme auf hohem Niveau ihre aktuelle Forschung vorstellen können. Also: Reichen Sie dem Komitee bitte frühzeitig Ihren interessanten Symposienvorschlag zur Gestaltung einer ansprechenden Tagung ein.

Die Tagung wurde zum dritten Mal in Kooperation mit Martin Göpferts Arbeitsgruppe als lokalem Organisator durchgeführt. Deren Erfahrungen aus 2015 und 2017 hat die Beteiligten noch effektiver agieren lassen und die Kooperation mit der NWG-Geschäftsstelle noch weiter optimiert. Erfreulicherweise wird die Mannschaft um Martin Göpfert auch die Tagung 2021 mittragen – never change a winning team! Die Teilnehmerbefragung bestätigt die hochwertige Organisation des Meetings (Abbildung 5). Durchschnittlich 80 % der Teilnehmer bewerteten die Organisationspunkte mit zufriedenstellend oder besser, 60 % sogar mit gut bis exzellent. Auch das Abendbuffet bekam in 2019 bessere Bewertungen als die Jahre zuvor. Es wurden drei unterschiedliche Buffets angeboten, eines davon erstmals von der Gemeinnützigen Hertie-Stiftung vor der Hertie-Lecture, welches sich kulinarisch an der Nationalität des Sprechers orientierte. Die Gemeinnützige Hertie-Stiftung plant auch in 2021 ein Buffet anlässlich ihrer gleichnamigen Lecture auszurichten. Es gibt kaum eine Tagung ähnlich internationalen Formats, die in diesen Punkten mithalten kann. Das stetig wachsende Interesse der Industrieaussteller an der Göttinger Tagung (69 im Jahr 2019) ermöglicht es uns, kostenlose Leistungen wie Kaffeepausen oder Abendbuffets anzubieten. Die zur Verfügung stehende Ausstellungsfläche wurde übrigens

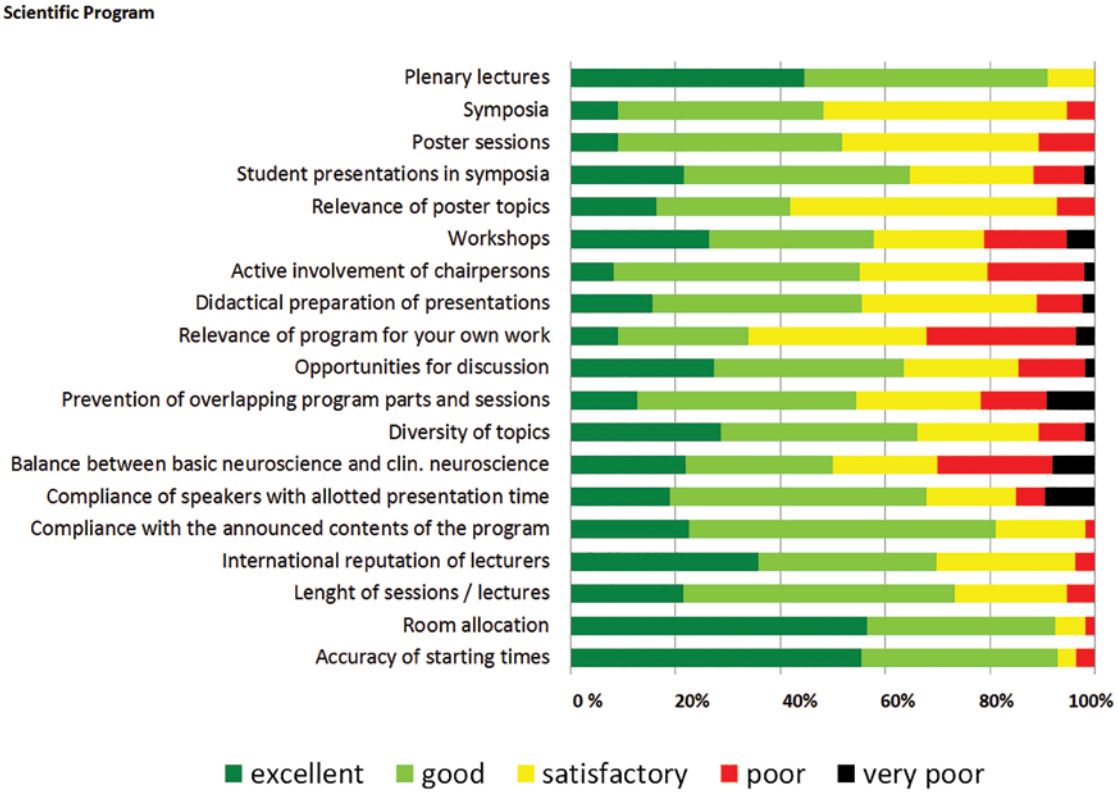


**Abb. 4:** Bewertung des wissenschaftlichen Programms durch die Teilnehmer

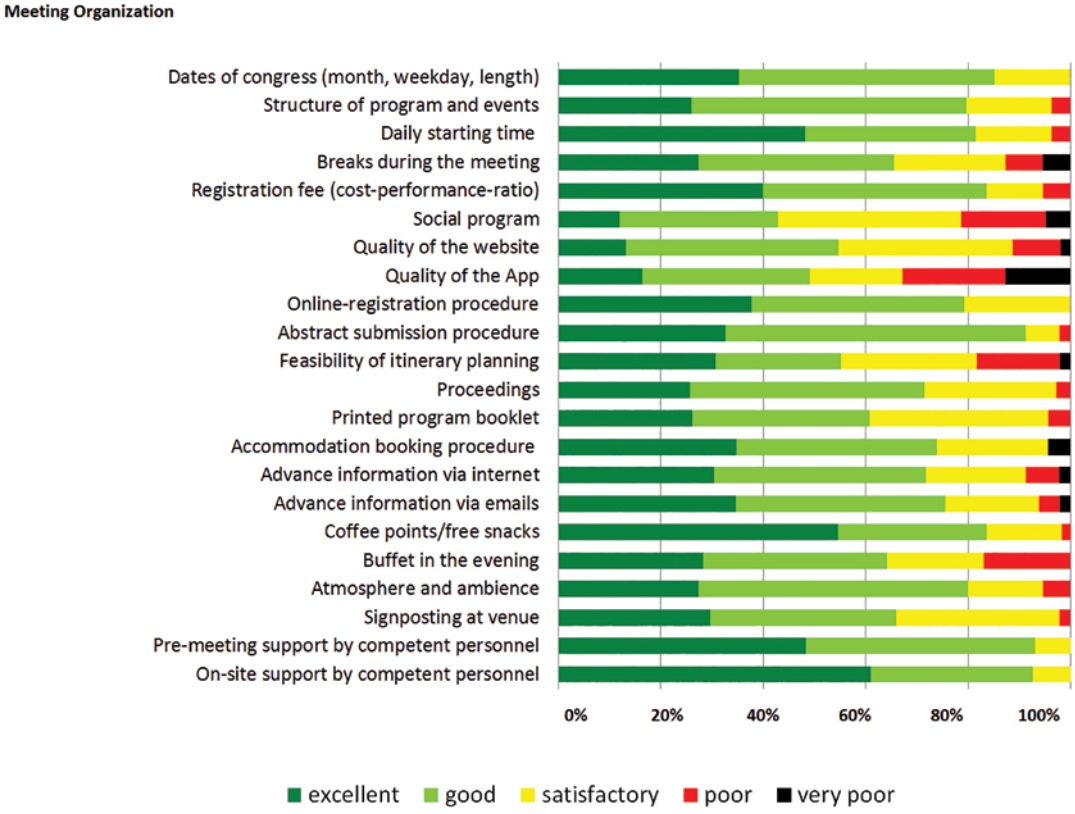


**Abb. 5:** Bewertung der Organisation der Tagung durch die Teilnehmer

wieder voll ausgeschöpft. Den Industriepartnern gilt unser besonderer Dank, ebenso der Deutschen Forschungsgemeinschaft, die die Tagung erneut großzügig mit Reisekostenzuschüssen für die ausländischen Redner unterstützte. Verbesserungsbedarf gibt es seitens der Nutzer in erster Linie bei der App, die wir erstmals angeboten haben. Deren Qualität bewerteten etwa ein Drittel der abstimmenden Teilnehmer mit ‚poor' bis ‚very poor'.

Zum Abschluss, frei nach Sepp Herberger: nach der Tagung ist vor der Tagung. Bitte merken Sie sich die kommende Tagung 2021 vor und halten Sie die Tage vom 24.–27. März 2021 frei. Wir sehen uns, schaun mer mal.

## Methodenkursprogamm 2020

**February 11–13, 2020: Transcranial Brain Stimulation in Research and Clinic: Best Practice**
**Venue:** Klinik für Klinische Neurophysiologie, Universitätsmedizin Göttingen, Robert-Koch-Strasse 40, 37075 Göttingen
**Registration Deadline: February 1, 2020**
**Topics:** transcranial magnetic-, direct current- alternating current and random noise stimulation, theoretical background of the stimulation, animal models, modelling of current flow in the brain, research and clinical applications; neuronavigation, neuronal oscillations, cognition, ethical aspects of transcranial stimulation
**Organisation and registration**: apl. Prof. Andrea Antal, Tel.: +49 (0)551 398461, AAntal@gwdg.de

**March 2–4, 2020: Comparative Anatomy and Pathology of the Rodent and Human Brain**
**Venue:** Section Clinical neuroanatomy, Neurology, Center for Biomedical Research (ZBF), Helmholtzstr. 8/1, 89081 Ulm
**Registration Deadline: February 22, 2020**
**Topics:** Overview of the anatomy of the rodent and human brain and spinal cord; hands-on-lab sessions for introduction into neuroanatomical techniques to study the human brain; pathological neuroanatomy of neurodegenerative disorders including but not limited to Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis
**Organisation and registration:** Prof. Dr. Deniz Yilmazer-Hanke, Tel. (office): +49 (0)731 500 63157, (lab): +49 (0)731/500 63158, deniz.yilmazer-hanke@uni-ulm.de

**March 5–6, 2020: Pathoanatomy of the human central nervous system**
**Venue:** Section Clinical neuroanatomy, Neurology, Center for Biomedical Research (ZBF), Helmholtzstr. 8/1, 89081 Ulm
**Registration deadline: February 22, 2020**
**Topics:** Introduction to neuroanatomical techniques to study the neuroanatomy of the human brain including hands-on laboratory sessions; pathological anatomy, histology and histopathology of the human brain and spinal cord in neurodegenerative diseases; staging of pathological changes in Alzheimer's and Parkinson's Disease and Amyotrophic Lateral Sclerosis
**Organisation and registration:** Prof. Dr. Deniz Yilmazer-Hanke, Tel.: (Office): 0731/500-63157, Tel.: (Lab): 0731/500-63158, deniz.yilmazer-hanke@uni-ulm.de

**March 23–30, 2020: From Neuroscience to Machine Learning and Back**
**Registration Deadline: February 16, 2020**
**Venue:** Bernstein Center Freiburg, Hansastraße 9a, 79104 Freiburg
**Topics:** deep learning for EEG; brain computation and learning: lessons from biological data; reinforcement learning and neurorobotics; deep learning in spiking neural networks; biologically plausible learning rules (backpropagation and brain, learning: brain vs AI.)
**Organisation and registration:** Dr. Birgit Ahrens, Tel.: +49 (0)761 203 9575, nwg-course@bcf.uni-freiburg.de

**March 26–27, 2020: Behavioral Testing in Rodents: from Cognition, Motor Function, Emotion, Anxiety to Pain**
**Venue:** Interdisciplinary Neurobehavioral Core INBC, University of Heidelberg INF 515; 69120 Heidelberg
**Registration deadline: March 15, 2020**
**Topics:** Behavioral testing in rodents: from cognition, motor function, emotion, anxiety to pain. A hands-on course. **Organisation and registration:** Dr. Claudia Pitzer, Tel.: +49 (0)6221 1858504, Claudia.Pitzer@pharma.uni-Heidelberg.de, http://www.medizinische-fakultaet-hd.uni-heidelberg.de/Home.111344.0.html

**March 30 – April 3, 2020: Neurobiological Practical Course – HEARING**
**Registration Deadline: February 28, 2020**
**Venue:** Universitäts-HNO-Klinik, Elfriede-Aulhorn-Str. 5, 72076 Tübingen
**Topics:** in-vivo Electrophysiology of Patch Clamping of Outer Hair Cells, in-situ Hybridisation, Microdissection of the Cochlea, Otoacoustic Emission
**Organisation and registration:** Univ.-Prof. Dr. Prof. h.c. A.W. Gummer, Universitäts-HNO-Klinik, Sektion Physiologische Akustik und Kommunikation, Tel.: +49 (0) 7017 2988191 anthony.gummer@uni-tuebingen.de, http://www.cochlea.uni-tuebingen.de/

**May 6–8, 2020: Cellular Models of Neurodegenerative Diseases**
**Registration Deadline: December 31, 2019**
**Venue:** Sektion für Translationale Neurodegeneration, Klinik für Neurologie, Universitätsmedizin Rostock, Gehlsheimer Strasse 20, 18147 Rostock
**Topics:** isolation of fibroblasts; production and culture of patient-derived IPS cells (including principles of CRISPR/CAS9); differentiation of IPS cells to neurons and glial cells; Live Cell Imaging of different cell organoids using baculovirus
**Organisation and registration:** Prof. Dr. Dr. Andreas Hermann, Frau Bianca Hartung; Sektion für Translationale Neurodegeneration „Albrecht Kossel"; Klinik für Neurologie, Rostock, Tel.: +49 (0)381 494-9541: email: sektionsleiter.akos@med.uni-rostock.de

**July 27–31, 2020: 4th Modelling Symposium: Introducing Deep Neural Networks**
**Registration Deadline: March 31, 2020**
**Venue:** Otto-von-Guericke University Magdeburg, G28 (R 027), 39106, Magdeburg
**Topics:** A hands-on course about applied deep learning covering: machine learning basics, common building blocks, design patterns and architectures (e. g. CNNs, RNNs, attention mechanisms etc.), common applications including image, audio and text processing, optimisation and regularization techniques, introspection and model diagnosis, model compression and transfer learning, best practices and general workflows (https://www.noesseltlab.org/events-presentations/4th-modelling-symposium/)
**Organisation and registration:** Dr. Felix Ball, OvG Universität Magdeburg, Institut für Psychologie – Biologische Psychologie, events.biopsych@ovgu.de

**September 21–25, 2020: Imaging and Optical Stimulation Techniques in Neuroscience**
**Venue:** LIN Leibniz Institute for Neurobiology, Brenneckestraße 6, 39118 Magdeburg
**Registration deadline: June 30, 2020**
**Topics:** Hands-on introduction into advanced optical techniques to study neuronal function: Optical voltage imaging, optogenetic stimulation of neuronal circuits, metabolic imaging (NADH), multi-channel STED, light-sheet microscopy, ex-vivo & in-vivo calcium-imaging (2P/1P), FLIM/FRET & MIET of biosensors, image analysis
**Organisation:** P. Bauer, R. Herrera-Molina, O. Kobler, S. Mikulovic, J. Pakan, M. Prigge, T. Stöter, A. Weber, W. Zuschratter
**Registration:** Torsten Stöter, Combinatorial NeuroImaging Core Facility (CNI), Leibniz Institute for Neurobiology, Tel.: 0391 6263 92171, cni-reg@lin-magdeburg.de

**Oktober 1–2, 2020: Tübingen Systems Neuroscience Symposium 2020**
**Registration deadline: September 1, 2020**
**Venue:** MEG-Zentrum der Universität Tübingen, Otfried-Müller-Straße 47, 72072 Tübingen
**Topics:** The 2020 Tübingen Systems Neuroscience Symposium brings together leading international researchers in the field of systems neuroscience. Topics range from neurophysiological testing in animals to functional imaging in humans (MEG, EEG, fMRI). One focus of the symposium is the presentation of state of the art methods. The talks target students and researchers with profound previous knowledge.
**Organisation and Registration:** Prof. Dr. Christoph Braun, Tel: 07071 29 87706, Fax: 07071 29 5706, E/Mail: christoph.braun@uni-tuebingen.de

Details unter https://nwg-info.de/aktivitaeten/kurse_workshops/2020

**Wissenschaftlicher Koordinator:** Prof. Dr. Hans Werner Müller, Labor für Molekulare Neurobiologie, Neurologische Klinik, Universitätsklinikum Düsseldorf, Moorenstr. 5, D-40225 Düsseldorf, E-Mail: HansWerner.Mueller@uni-duesseldorf.de

# Klaus Tschira Stiftung – neue Hauptförderin von www.dasGehirn.info

Am 31. August 2019 endete für www.dasGehirn.info die elfjährige Förderung durch die Gemeinnützige Hertie-Stiftung. Ihrer großzügigen Unterstützung ist es zu verdanken, dass die NWG in Projektpartnerschaft mit der GHS und dem Zentrum für Kunst und Medien Karlsruhe das Portal gründen konnte und mit großem Erfolg betreibt: dasGehirn.info ist mit einer Reichweite von bis zu 200.000 monatlichen Nutzern eine feste Größe in der Vermittlung neurowissenschaftlicher Erkenntnisse.

Glücklicherweise ist durch die Klaus Tschira Stiftung gGmbH (KTS) die Fortsetzung des gemeinnützig betriebenen Portals für weitere drei Jahre gewährleistet. Mit der Übernahme der Grundförderung sichert die KTS damit eines der wichtigsten Projekte der Wissenschaftskommunikation der letzten Jahre. Und Wissenschaftskommunikation gehört neben der Förderung von Forschung und Bildung zu den Förderzielen, denen sich die KTS verschrieben und einen Namen in der Fördererlandschaft gemacht hat. So ist etwa KlarText – der Preis für Wissenschaftskommunikation, verliehen für verständliche Wissenschaft, nicht nur unter Neurowissenschaftlern ein vertrauter Name und begehrter Preis. Ein weiteres Beispiel für ihr Engagement, Wissenschaft in die Gesellschaft zu tragen, ist das Nationale Institut für Wissenschaftskommunikation (NaWik) in Karlsruhe, dessen Mitbegründerin die KTS ist. Hier erwerben Wissenschaftler das Handwerkzeug, um erfolgreich Kommunikatoren ihrer eigenen Arbeit zu werden. Auch mit dem science media center hat die KTS eine Schnittstelle zwischen Wissenschaft und Gesellschaft geschaffen, um schnell fundierte Antworten auf gesellschaftlich aktuell diskutierte Themen zu geben, Ereignisse einzuordnen. Die KTS sucht nach Wegen, Wissenschaft aus der Expertennische in das Licht gesellschaftlicher Öffentlichkeit zu holen und bricht damit eine Lanze für eine mündige Gesellschaft.


Die Übernahme der Projektförderung durch die KTS bedeutet für das Portal dasGehirn.info Anerkennung und Bestätigung von Experten der Wissenschaftskommunikation mit dem verpflichtenden Auftrag, dieses einmalige Projekt mit gleichbleibend hoher Qualität und Anspruch weiterzuführen. Dies ist für die NWG eine Verpflichtung. Mit der Klaus Tschira Stiftung hat die NWG und dasGehirn.info einen idealen Verbündeten an der Seite.

Solveyg Blanke (s.blanke@dasgehirn.info)

# Neueintritte

Folgende Kolleginnen und Kollegen dürfen wir als Mitglieder der Neurowissenschaftlichen Gesellschaft begrüßen:

Johne, Marie (Hannover)
Jung, Felix (Stockholm, Schweden)
Martelli Dr., Carlotta (Mainz)
Protzmann, Jil (Solna, Schweden)

Der Mitgliedsstand zum 15. September 2019 beträgt 2.270 Mitglieder.

## The young section of the NWG gains momentum
## jNWG Kick-off Meeting (September 13 – 15, 2019)

jNWG had its first meeting at the Leibniz Institute for Neurobiology in Magdeburg on September 13 – 15, 2019, marking the kick-off of a new section of the German Neuroscience Society. Our new members spent 3 days brainstorming and organizing future goals and current channels of communication.

Our mission is to represent young neuroscientists within the society. We would like to bolster early scientific careers and provide a network for outreach and collaboration.

The meeting highlight were the entertaining and instructive career talks by our guest speakers Esther Kühn (IKND & DZNE Magdeburg), NWG vice president Christine Rose (Uni Düsseldorf), Matthias Prigge (LIN Magdeburg), Eckart Gundelfinger (LIN Magdeburg) and special guest NWG president Albert Ludolph (Uniklinik Ulm).

We accomplished setting up means of communication, both internally on slack & trello as well as a twitter account and a shiny new website. We also got creative designing a new logo and flyers and started collecting ideas on our first early career scientists meeting next year. Stay tuned for more info on this!

Katrina Deane (Katrina.Deane@lin-magdeburg.de) and Sophie Seidenbecher (seidenbecher@dandrite.au.dk)

**Fig. 7:** Intense discussions and brain storming

**Fig. 8:** Group photo

## NFDI Neuroscience: advocating cross-community data management in neuroscience
## NFDI Neuroscience Consortium Workshop (September 20, 2019)

Ever wondered how to get your data to a collaborator at a different university? Or how to store it with enough information, such that the next PhD student can continue your project? Maybe even just how to make sense of your complex data? Then there's help looming at the horizon, since the so-called 'NFDI Neuroscience' is gathering pace.

The NFDI Neuroscience (Nationale Forschungsdaten-Infrastruktur) consortium led by committed neuroscientists around Michael Denker (Forschungszentrum Jülich), Alexandra Stein (Bernstein Coordination Site) and Thomas Wachtler (German Neuroinformatics Node, LMU Munich) is specifically focusing on needs of neuroscientists and intends to address all of the above issues. To do so, it will bring together researchers and technology providers to develop processes for data management making your daily work easier and enabling you to sustain, share and reuse data. Additionally, this will facilitate large-scale studies using existing data and extract the maximum information, thereby tipping the cost-benefit-ratio of research and funding in favor of more results. In a nutshell, the 'primary goal is to improve science', as Thomas Wachtler puts it.

Many labs or sub-communities in neuroscience already use existing data management tools or have developed their own services. Therefore, the first aim of the consortium is to collect and map the community resources

to establish a dialogue discussing standards for data and metadata acquisition, naturally facing the diversity of technologies employed in neuroscience.

On September 20th, and thereby about one year after the successful NFDI Neuroscience kick-off, a first Community workshop was held at the TU Berlin, which was also joined by the jNWG. The meeting was dedicated to discuss current problems in data management in neuroscience, and several tool providers and neuroscientists debated the topics of storage, standardization, data rights, existing and wished-for solutions for data handling as well as benefits and reward-systems for data sharing.


Until October next year, NFDI Neuroscience will complete a community survey and submit a DFG grant proposal to get funding for the establishment of a German neuroscience data management network, built on existing and newly developed solutions addressing the needs of neuroscientists. If you're curious, have a look at https://nfdi-neuro.de/, for more general information on the NFDI initiative please also check https://www.dfg.de/foerderung/programme/nfdi/ and http://www.rfii.de/de/themen /.

Finally, if you have a well-working data management system in your lab or experience a dire need for one, reach out to NFDI Neuroscience! You can get involved by giving the NFDI-Neuroscience your impression and ideas of what's out there and what is still missing by taking their survey: https://nfdi-neuro.de/contributions.html

Andreas Ritzau-Jost (Andreas.Ritzau-Jost@medizin.uni-leipzig.de) und Sophie Seidenbecher (seidenbecher@dandrite.au.dk)

## Stipendien für das FENS Forum of European Neuroscience (Glasgow, UK, 11. – 15. Juli 2020)

FENS Federation of European Neuroscience Societies

Wie schon in den vergangenen Jahren stellt die Neurowissenschaftliche Gesellschaft auch diesmal wieder Stipendien in Höhe von 500 € für die Teilnahme am 12. Forum of European Neuroscience in Glasgow im Sommer 2020 zur Verfügung. Die Auswahl trifft ein Komitee aus NWG-Vorstandsmitgliedern.

Für eine Bewerbung sind folgende Kriterien zu erfüllen:
- Bewerben können sich Promovierende und junge Postdocs,
- die zum Zeitpunkt der Bewerbung nicht älter als 35 Jahre sind,
- die mit einem eigenen Beitrag teilnehmen und Erstautor sind,
- und die NWG-Mitglied sind, egal ob sie im In- oder Ausland leben und arbeiten.

Die Bewerbung muss über die Homepage der NWG (https://nwg-info.de/de/karriere/stipendien/fensforum/) eingereicht werden. Folgende Unterlagen sind auf Deutsch oder auf Englisch einzureichen:
- Bewerbungsschreiben (max. 3000 Zeichen inkl. Leerstellen)
- Lebenslauf (max. 3000 Zeichen inkl. Leerstellen)
- Publikationsliste (falls vorhanden)
- Kopie des beim FENS Forum präsentierten Abstracts (max. 3000 Zeichen inkl. Leerstellen)
- Ein kurzes Unterstützerschreiben

Die Bewerbung um ein Stipendium ersetzt NICHT die Registrierung für das FENS Forum. Diese muss unabhängig von der Stipendienbewerbung durchgeführt werden.

**Bewerbungsschluss ist der 3. Februar 2020.**

# Ausblick

Lübke, Joachim/Rollenhagen, Astrid
**Synapses: Multitasking Global Players in the Brain**

Pohlkamp, Theresa
**Apolipoprotein E: Cholesterol metabolism and Alzheimer's pathology**

Edwin Thanarajah, Sharmili/Tittgemeyer, Marc
**Food reward and gut-brain signaling**

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# Neurowissenschaftliche Gesellschaft e.V.

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Hiermit erkläre ich meinen Beitritt zur Neurowissenschaftlichen Gesellschaft e.V.

**Eintrag in das Mitgliederverzeichnis**

Name

Vorname

Titel

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Universität/Institut/Firma

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**Privatadresse**

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PLZ, Ort

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**Ich unterstütze den Antrag auf Beitritt zur Neurowissenschaftlichen Gesellschaft e.V.:**

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Neurowissenschaftliche Gesellschaft e.V.
Stefanie Korthals
Max-Delbrück-Centrum für Molekulare Medizin
Zelluläre Neurowissenschaften
Robert-Rössle-Straße 10

13092 Berlin

**Ich optiere für folgende 2 Sektionen:**
(bitte ankreuzen)

- ☐ Verhaltensneurowissenschaften
- ☐ Zelluläre Neurobiologie
- ☐ Entwicklungsneurobiologie und Neurogenetik
- ☐ Neuropharmakologie und -toxikologie
- ☐ Systemneurobiologie
- ☐ Molekulare Neurobiologie
- ☐ Klinische Neurowisschenschaften
- ☐ Computational Neuroscience
- ☐ Kognitive Neurowissenschaften

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# Call for Symposia

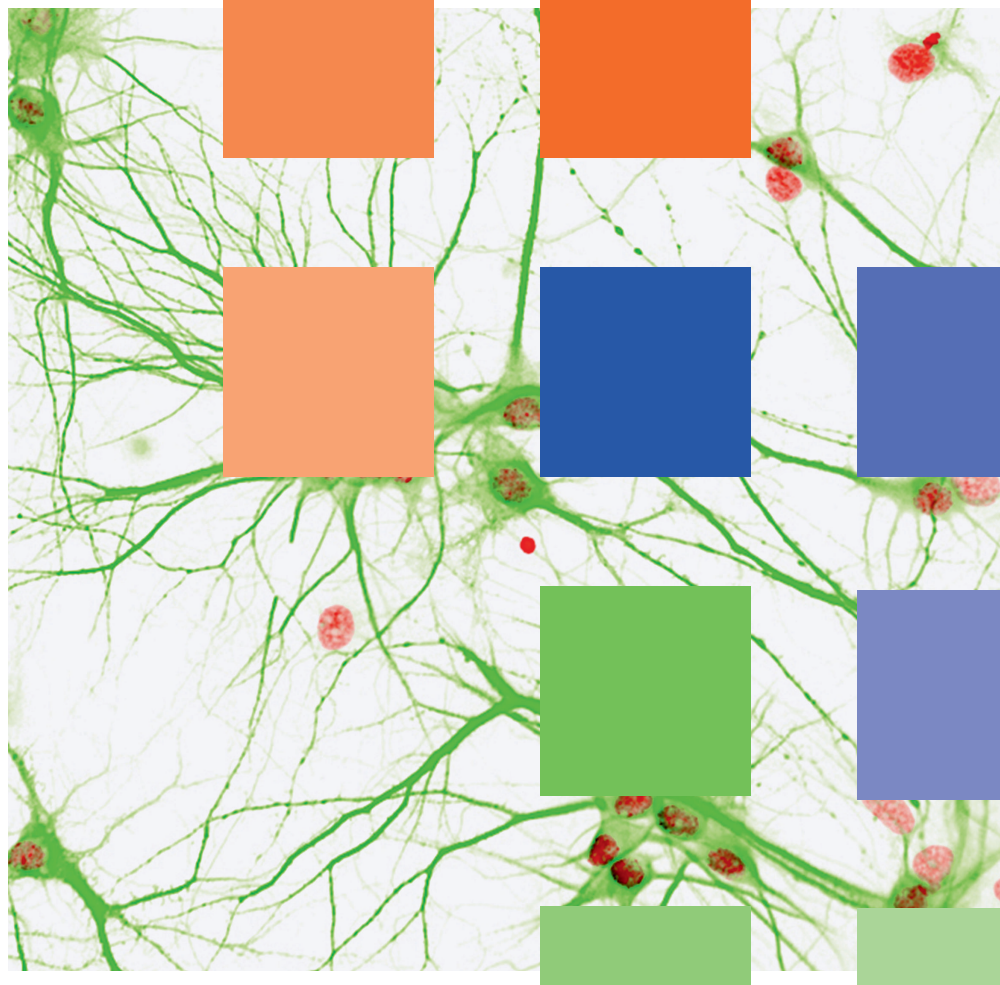
Symposia dealing with all areas of neuroscience research are invited. Applicants should submit a proposal containing the title of the planned symposium, the name(s) and address(es) of the organizer(s), a short description of the aims of the symposium and the names, addresses and topics of the speakers to be invited. The NWG strives to increase the proportion of women as organizers and speakers of symposia. The gender distribution within each proposal will therefore be one selection criterion. For more information please visit the Society's website: **www.nwg-info.de**

**Deadline for submission of symposium proposals: February 17, 2020**

NWG

NeuroWissenschaftliche Gesellschaft

German Neuroscience Society



**Program Committee:**
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Prof. Dr. Mathias Bähr
Prof. Dr. Ansgar Büschges
Prof. Dr. Veronica Egger
Prof. Dr. Eckhard Friauf
Prof. Dr. Martin Göpfert
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Prof. Dr. Christine Rose
Sophie Seidenbecher
Prof. Dr. Christian Steinhäuser
Prof. Dr. Petra Wahle
Prof. Dr. Christian Wegener
Prof. Dr. Melanie Wilke

**Local Organizer:**
Prof. Dr. Martin Göpfert
Zelluläre Neurobiologie
Schwann-Schleiden-Forschungszentrum
Julia-Lermontowa-Weg 3
37077 Göttingen
mgoepfe@gwdg.de

**Organization:**
Neurowissenschaftliche Gesellschaft e.V.
Max Delbrueck Center for Molecular Medicine (MDC)
Berlin-Buch
Robert Roessle Str. 10
13092 Berlin
Phone: +49 30 9406 3127
Fax: +49 30 9406 2813
E-Mail: korthals@mdc-berlin.de
Homepage: www.nwg-info.de

# 14th Göttingen Meeting of the German Neuroscience Society

## March 24–27, 2021

**Stipends:** The German Neuroscience Society will provide stipends for young qualified researchers. Details will be announced at **www.nwg-goettingen.de/2021**

The programs of the last meetings are available at **www.nwg-info.de/meetings/jahrestagung/archive**

Gestaltung: Eta Friedrich | Abb.: Jochen Meier, Braunschweig

Neurowissenschaftliche Gesellschaft e.V.

# Neurowissenschaften
## in der gymnasialen Oberstufe

Schuljahr

*2019/2020*

https://nwg-info.de/

NWG
NeuroWissenschaftliche Gesellschaft
German Neuroscience Society

**Die Neurowissenschaftliche Gesellschaft e.V. (NWG) bietet bundesweit kostenlose Fortbildungsveranstaltungen für (Oberstufen-)LehrerInnen an. Interessierte LehrerInnen sind herzlich zur Teilnahme eingeladen.**

## Programmübersicht

**27. September 2019 | Berlin**
Serotonin, Sport und die Neubildung von Nervenzellen
Kontakt: Dr. Luiza Bengtsson
Tel.: 030 94062513
E-Mail: LaborTrifftLehrer@mdc-berlin.de

**10. Oktober 2019 | Freiburg**
Neuronale Steuerung in der Motorik
Kontakt: Fiona Siegfried
Tel.: 0761 203-9549
E-Mail: siegfried@bcf.uni-freiburg.de

**30. Oktober 2019 | Koblenz**
Über das Vergessen lernen – Alzheimer im Biologie-Unterricht
Kontakt: Prof. Dr. Stefan Kins
Tel.: 0631 2052106/2107
E-Mail: l.hanke@biologie.uni-kl.de

**8. November 2019 | Berlin**
Organoide des menschlichen Gehirns (alias mini-Gehirn) und die Regulation der Genexpression
Kontakt: Dr. Luiza Bengtsson
Tel.: 030 94062513
E-Mail: LaborTrifftLehrer@mdc-berlin.de

**12. November 2019 | Berlin**
Neues aus der Hirnforschung
Kontakt: Prof. Dr. Helmut Kettenmann / Helga Fenz
Tel.: 030 94892931
E-Mail: h.fenz@campusberlinbuch.de

**13. Februar 2020 | Tübingen**
Aktive Orientierung
Kontakt: Prof. Dr. Uwe Ilg
Tel.: 07071 2987602 (Hertie-Institut)
Tel.: 07071 2982377 (Schülerlabor)
E-Mail: uwe.ilg@uni-tuebingen.de

**13. Februar 2020 | Oldenburg**
Neurosensorik und Neurodegeneration „Neue Erkenntnisse zu Fetten, Sinnen und dem Zelltod“
Kontakt: Prof. Dr. Anja Bräuer
Tel.: 0441 7983995
E-Mail: silvia.ellinghaus@uni-oldenburg.de

**14. Februar 2020 | Heidelberg**
Das junge Gehirn – Entwicklung, Reifung, Störungen
Kontakt: Prof. Dr. Andreas Draguhn / Susanne Bechtel
Tel.: 06221 544056
E-Mail: susanne.bechtel@physiologie.uni-heidelberg.de

**18. März 2020 | Leipzig**
Neue Entwicklungen in der Mikroskopie
Kontakt: Prof. Dr. Steffen Rossner / Dr. Max Holzer
Tel.: 0341 9725758 / 0341 9725759
E-Mail: rossn@medizin.uni-leipzig.de oder holm@medizin.uni-leipzig.de

Das Internetportal zum Thema Neurowissenschaften:

**https://www.dasGehirn.info**

**Neurowissenschaftliche Gesellschaft e.V.**
**Geschäftsstelle**
**Max Delbrück Centrum für Molekulare Medizin (MDC) Berlin-Buch**
**Robert-Rössle-Str. 10**
**13125 Berlin**
**Tel.: +49 30 94063127**
**Fax: +49 30 94062813**
**E-Mail: v.heinemann@mdc-berlin.de**

Für die Anmeldung zur jeweiligen Veranstaltung wenden Sie sich bitte an den lokalen Kontakt.

Weiteres Informationsmaterial für Lehrer finden Sie auf der Homepage der NWG:

**> Kosmos Gehirn als Download**
https://nwg-info.de/sites/nwg-info.de/files/media/pdf/kosmos-gehirn.pdf
**> Kleines Sachwörterbuch der Neurowissenschaften**
https://nwg-info.de/aktivitaeten/lehrerfortbildung/links/glossar
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https://nwg-info.de/aktivitaeten/lehrerfortbildung/links/skripte

Gestaltung: Eta Friedrich, www.et-a.de