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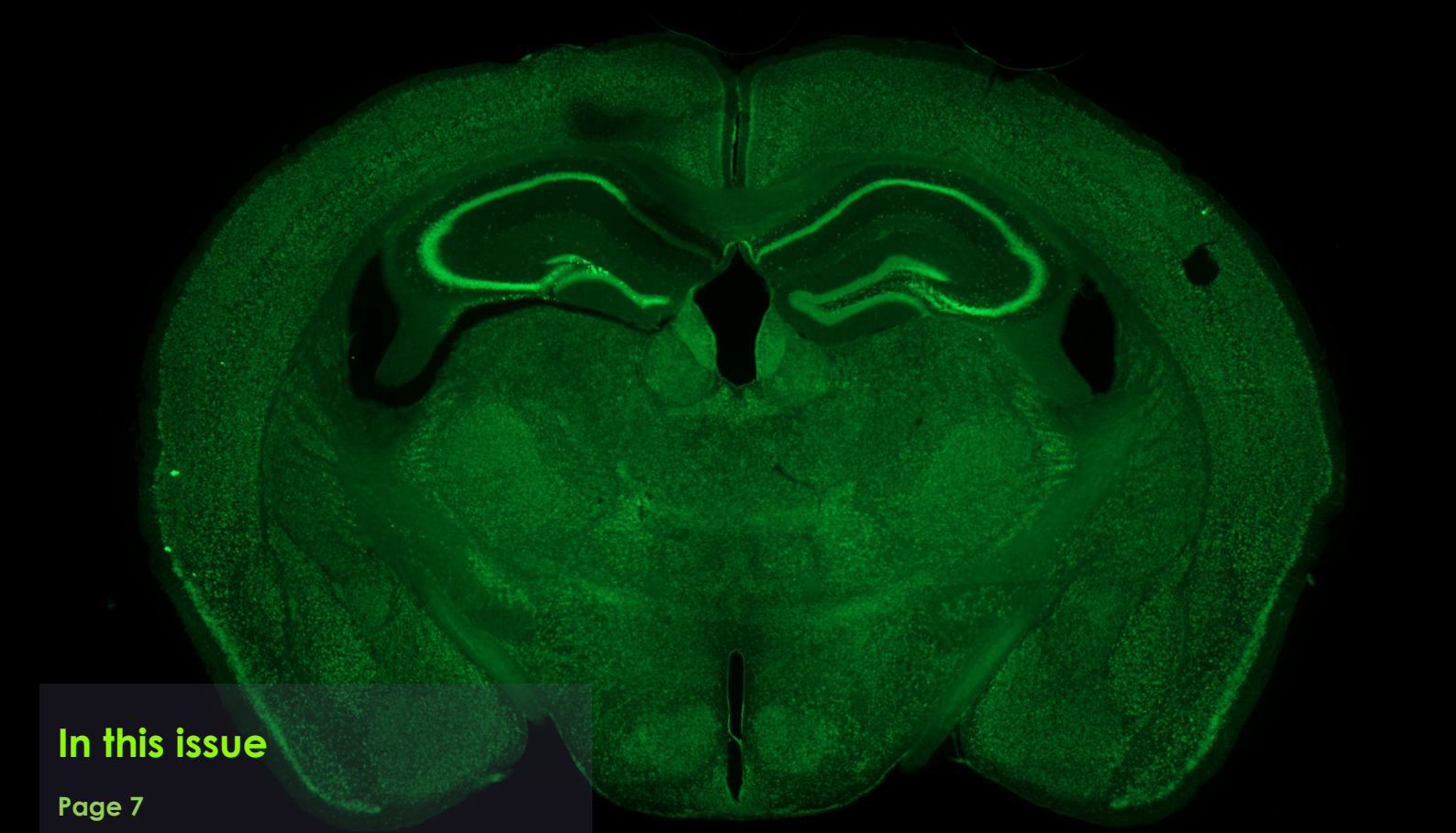

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Neurobiology of ADHD: the research story so far

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Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) is a complex pathophysiological disorder, which is currently restricted to symptom-based clinical diagnosis instead of biomarker-based one. While unravelling its etiology has been complicated, studies targeting the genetics, and functional and structural aberrations in cortical regions and networks implication in this disorder have gained momentum over the past two decades, in an effort to find putative ADHD biomarkers and potential therapeutic targets to treat the disorder with higher efficiency. This review aims to bring together some key studies to aid diagnostic and therapeutic efforts.

Keywords

Attention-Deficit/Hyperactivity Disorder, ADHD, prefrontal cortex, fMRI and genetics

Abbreviations

ADHD - Attention-Deficit/Hyperactivity Disorder

AN - Affective Network

CC - Corpus Callosum

CEN - Central Executive Network

dACC - Dorsal Anterior Cingulate Cortex

DAN - Dorsal Attention Network

DBH - Dopamine b-Hydroxylase

DMN - Default Mode Network

DRD4 - Dopamine D4 Receptor

DRD5 - Dopamine D5 Receptor

DSM-5 - Diagnostic and Statistical Manual of Mental Disorders, Fifth edition

FA - Fractional Anisotropy

fMRI - Functional MRI

GM - Grey Matter

GP - Globus Pallidus

GWAS - Genome-Wide Association Studies

HTR1B - Serotonin 1B Receptor

IMAGE - International Multisite ADHD Gene

NAc - Nucleus Accumbens

PFC - Prefrontal Cortex

SLC6A3 - Solute Carrier Family 6 Member 3

SLC6A4 - Solute Carrier Family 6 Member 4

SNAP 25 - Synaptosomal-Associated Protein 25

SNPs - Single-Nucleotide Polymorphisms

SS - Sagittal Stratum

SSN - Somato-sensory Network

VAN - Ventral Attention Network

WM - White Matter

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) - is a neurodevelopmental disorder that is defined by Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (DSM-5) as a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development [1]. It is usually diagnosed with worldwide prevalence rates of 5%–8% in school children but symptoms may persist into adulthood [3]. To be diagnosed with ADHD, patients must have symptoms that occur often and persist for six months, and at least some of these symptoms should present before the age of 7, causing significant impairment in social and school functioning [6].

There are three subtypes of ADHD based on the dominant symptom presentation: Inattentive Type, Hyperactive-Impulsive Type, and Combined Type for those with both symptoms [2]. Beyond this classification, ADHD is poorly understood, one of the reasons for which is a clinical heterogeneity with high rates of comorbidity with other disorders such as anxiety, depression and learning disabilities. It is estimated that around 60%–100% of children with ADHD exhibit at least one comorbid disorder [3].

Treatment for ADHD includes pharmacological and non-pharmacological interventions. Non-pharmacological therapies include behavioural therapy such as social skills training, meditation, hypnotherapy, as well as better quality of sleep and physical activity. Pharmacological treatments include stimulants (methylphenidate hydrochloride, lisdexamfetamine dimesylate, amphetamine sulphate and mixed amphetamine salts) as first-line treatment; and non-stimulants such as selective noradrenaline reuptake inhibitors (atomoxetine, viloxazine) and α2 adrenergic receptor agonists (guanfacine hydrochloride, clonidine hydrochloride) as the second-line medications [5, 7]. However, one study done by Jeff Schein et al. in 2022 showed that about 95.2% of participants treated with stimulants (93.7%), non-stimulants (17.9%), and combination therapy (38.6%), reported experiencing an average 5.8 symptoms associated with ADHD/treatment-related side effects, such as insomnia and other sleep disturbances (47.9%), anxiety and panic attacks (47.7%), depressed mood (45.6%), and emotional impulsivity/mood lability (45.1%) [8].

Stimulants used for ADHD treatment indicate a dopamine/norepinephrine deficit as the neurochemical basis of ADHD. Specific brain regions such as the prefrontal cortex (PFC) and other subcortical regions have been implicated in disease pathology. Moreover, functional MRI (fMRI) studies have shown differences in the structural development and functional activation of these regions in patients with ADHD [4, 5]. ADHD has been associated with structural, functional and genetic factors but the exact pathophysiology of ADHD is still not clear.

In this review we talk about ADHD neurobiological basis, specifically informed by studies in genetics and structural and functional neuroimaging, and bring to the forefront all that is known about this disease so far at different scales, to better aid diagnosis, symptom-management and therapeutic strategies for ADHD.

Methods

For this review, original articles, reviews and studies were accessed through Google Scholar (https://scholar.google.fr/) and PubMed (https://pubmed.ncbi.nlm.nih.gov/). The keywords used for the search were: “Neurobiology +ADHD +review”, “Genetics +ADHD +review”, and “Pharmacology +ADHD”. Reviews from 2010 and onwards were selected and research articles and studies were found through the references of these reviews. Studies articles from 2010 or onwards were retrieved from these reviews, but exceptions were made for seminal articles proposing important relevant theories.

Results and discussion

Genetics

ADHD has a genetic contribution, and twin and family studies of ADHD showed total heritability ranging about 70%–80% [10, 39], but the mechanism of action is not completely understood [6]. A 2022 large-scale genome-wide association study (GWAS) identified that 14% of phenotypic variation in ADHD is attributed to common genetic variants, specifically single-nucleotide polymorphisms (SNPs). This research also showed that around 7000 common variants can explain 90% of the phenotypic variation, confirming the polygenic architecture and base of ADHD [10]. The polygenicity of ADHD can also be supported by the fact that ADHD-like symptoms sometimes are exhibited by patients with established neurogenetic disorders, such as Neurofibromatosis-I, Turner Syndrome and Williams Syndrome, because the effects of genetic abnormalities may give rise to common effects downstream in the biological pathways or neural circuits, resulting in the presentation of ADHD-like symptoms [6].

Gene studies have provided substantial evidence linking potential alleles on chromosomes 5p13, 6q12, 16p13, 17p11, and 11q22-25 to ADHD [6]. Additionally, several meta-analyses suggest a strong association between ADHD and specific genes, including the dopamine D4 receptor (DRD4), dopamine D5 receptor (DRD5), dopamine β-hydroxylase (DBH), synaptosomal-associated protein 25 (SNAP-25), serotonin transporter (SLC6A4), serotonin 1B receptor (HTR1B), and dopamine transporter (SLC6A3) (Table 1) [6, 13]. The genes may have a role in modulating the ADHD phenotype rather than causing it, for instance, GWAS studies failed to report any significant associations between the DAT1 gene, another gene implicated in the ADHD etiology [12]. Therefore, a plausible genetic hypothesis for ADHD is a mixture of dominant and recessive major genes that act with complex polygenic transmission patterns. A majority of ADHD molecular genetics was published at the International Multisite ADHD Gene (IMAGE) project in which 51 genes were analysed for association with ADHD.

Structural Neuroimaging

An early hypothesis in the field pinned behavioural inhibition and sustained attention as two aspects where cognitive deficits are seen in ADHD subjects [14]. Circuits and brain regions involved in behavioural planning, attention and executive functions have since gained popularity in structural and functional studies for ADHD. These include the striatum (consisting of the caudate nucleus, putamen, nucleus accumbens (NAc) and globus pallidus (GP)), the lateral PFC, and the dorsal anterior cingulate cortex (dACC) [9, 15, 16]. The lateral PFC is especially sensitive to concentrations of dopamine and norepinephrine. A functional monoaminergic neurotransmission subserves cognitive functions that are found to be impaired in ADHD, and this has also been confirmed with treatments targeting these systems. The dACC is important for complex cognition such as error detection and reward-based decision-making, which are found to be impaired in ADHD [9]. Basal ganglia and cerebellum are two additional regions considered important in the control of voluntary actions and fine-motor skills, which are often impaired in subjects with ADHD, leading to motor deficits and delayed development of fine-motor skills [6, 17, 18].

Besides cortical regions, white matter irregularities studied with diffusion tensor imaging (DTI) and quantified predominantly with fractional anisotropy (FA, where a higher value means more coherent, ie, more myelinated white matter) in the commissural tracts, and tracts connecting the above mentioned regions, have also been studied in relation to ADHD [11].

Some key studies for structural and connectivity (cortical volume, developmental trajectories) irregularities have been summarised in Table 2. General findings point to a reduction in volume and grey matter (GM) in the whole cerebrum, PFC, striatum, cerebellum and dACC, and a reduction in myelination (from a lower FA score) in the corpus callosum (CC), sagittal striatum (SS) and the cerebellar peduncle.

Gene name	Protein function	Where is an genetic alteration	Role/effect
D4 receptor gene (DRD4)		a 7-repeat allele tandem repeat polymorphism in exon III	children with the 7-repeat allele had higher levels of retrospectively reported inattention symptoms
			7-repeat allele have demonstrated significantly better attention than subjects with fewer repeats
The Dopamine 5 Receptor (DRD5)		dinucleotide repeat at 5' (18.5 kb)	the risk allele was associated with lower hyperactivity scores
The Dopamine Transporter Gene (DAT, SLC6A3)	pumps the neurotransmitter dopamine out of the synaptic cleft back into cytosol	whole gene	eliminating SLC6A3 gene function leads to two features suggestive of ADHD: hyperactivity and deficits in inhibitory behaviour
Dopamine Beta-Hydroxylase (DBH)	DBH is the primary enzyme responsible for conversion of dopamine to norepinephrine	Taq1 restriction site polymorphism in intron 5	significant association with the A1 allele and ADHD symptom scores in children with Tourette's Syndrome (TS)
Monoamine Oxidase A (MAO-A)	The MAO-A enzyme moderates levels of norepinephrine, dopamine, and serotonin	30-bp pair tandem repeat in the promoter region	association with ADHD and particularly large effect in the subset of female cases
		4 and 5 repeat alleles of this promoter-region VNTR	significantly associated with ADHD in a sample of families
The Dopamine D2 Receptor (DRD2)		excess transmission TaqIA1 allele	strong association with ADHD
The Dopamine D3 Receptor (DRD3)		Ser9Gly exon 1 polymorphism and an intron 5MspI restriction site polymorphism	no evidence for association with ADHD
			heterozygosity at this polymorphism was associated with higher impulsivity scores
Catechol-O-methyltransferase (COMT)	COMT catalyses a major step in the degradation of dopamine, norepinephrine, and epinephrine	Val108Met polymorphism	no evidence of association with ADHD

Table 1. Summary of the genetic linkage studies with examples of the genes and their role in ADHD described in "Molecular genetics of attention deficit hyperactivity disorder" review by Stephen V. Faraone et al. (2010) [13].

Cerebellum	Balance, Fine motor control, Inhibitory control, Working memory	Smaller cerebellum*	19*, 20
		Smaller posterior-inferior cerebellar vermis**	26**
Dorsal anterior cingulate cortex (dACC)	Cognition, motor control, state of arousal	Decreased ACC volume	21
		Thinning of the ACC in adults with ADHD	27
Inferior Parietal Cortex	Heteromodal association cortex, attention and behavioural inhibition, language	Increased GM in bilateral inferior parietal cortices	28
		Cortical thinning in the right inferior parietal lobule in adults with ADHD	27
Cortical White Matter		Reduced total WM volume	20
Sagittal Stratum (SS)	Connects parietal, occipital, temporal and cingulate regions to thalamus and brainstem, Attention, memory, visual processing, reading, non-verbal processing	Increased FA in the left SS	29
Corpus Callosum (CC)	Main commissural fibres connecting primary motor and sensory areas, Attention and response inhibition	Decreased FA in the isthmus of the CC	30
	Commissural fibres for the occipital, parietal and temporal regions	Decreased FA in the splenium of CC	31
Cerebellar Peduncle	Connects cortical sensory and motor areas with pons and cerebellum, Fine motor control	Reduced FA	32
Frontostriatal WM	Connecting the prefrontal cortex with the striatum	Reduced FA but indifferent magnetization transfer ratio suggesting changes in microstructural organisation rather than myelination	33
Subgenual cingulum	Connects ACC to medial PFC, insula and amygdala, Connects nodes of default mode network	Positive association between FA of the subgenual cingulum, and symptom severity in male adolescents with ADHD*	34*

Table 2. Summary of structural aberrations found in ADHD patients as compared to controls. Key (*): study conducted in male subjects only, (**): study conducted in female subjects only.

Functional Neuroimaging

Beyond anatomical connectivity, functional connectivity characterised by temporally-correlated spontaneous activity of spatially-separated brain regions has also been studied. Connected regions form networks that can be active during task performance or at 'rest' (characterised using resting-state functional magnetic resonance imaging, rs-fMRI) such as default mode (DMN), central executive (CEN), ventral attention (VAN), dorsal attention (DAN), somato-sensory (SSN) and affective (AN) networks. Of these, DMN is considered to be primarily active during the resting state and deactivated during external stimulation [11].

One meta-analysis of rs-fMRI studies found hypoconnectivity within DMN, hyperconnectivity between DMN and CEN, and hypo- and hyperconnectivity between DMN and regions of AN (left superior temporal gyrus and cingulate cortex, respectively), hyperconnectivity between CEN and AN, and hyperconnectivity between AN and DMN (middle frontal gyrus) and CEN (dorsolateral PFC) [35]. Another meta-analysis added to these findings, by identifying regions of hypoconnectivity (between DMN regions and the posterior cingulate cortex) and hyperconnectivity (between DMN regions and dorsomedial PFC) within DMN, and by showing hyperconnectivity within CEN [36]. Together, these meta-analyses provide support for the theory that insufficient attenuation of DMN during tasks causes impairment in performance and attention [37]. The altered connectivity between networks supports the multi-network model of psychopathology [38]. Finally, delayed development of network organisation in ADHD-affected youth brings these observations into a developmental frame [11].

Conclusions

This review aimed to present recent advances from functional and structural neuroimaging as well as genetic studies of ADHD, in an effort to converge on an understanding of the disorder. Studies on ADHD genetics reveal that genes integral to the monoaminergic transmission systems seem to modulate the disorder phenotypes, providing a model for polygenic susceptibility for ADHD. Meanwhile, structural neuroimaging studies highlight the regions such as the PFC, striatum and dACC affected by the development of the disorder, and functional analyses implicate the altered connectivity within and between functional networks such as DMN and CEN for the characteristic cognitive deficits. While our understanding of the neurobiology of ADHD has certainly improved immensely over the past two decades, some critiques still remain. Some studies have only been conducted in males, highlighting the need for more gender-balanced study designs. A lack of longitudinal studies, with or without medicated study cohorts also holds us back from a developmental perspective of the disorder in the lifetime of a patient. With precise knowledge about pathophysiology and development of ADHD, more targeted treatment with fewer adverse effects can be developed.

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Seeing neuroscience in the light of evolutionary theory.

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The nervous systems of extant (i.e. still in existence) animal species present extraordinary diversity, which reflects and should be understood through the equally long evolutionary paths they have undergone. Putting neuroscience back in an evolutionary context is, therefore, key to understanding the emergence and diversification of neural processes, as well as the general mechanisms which rule them. Regardless, most neuroscientists working away from paleontology departments seldom encounter the word "evolution" near to "neuroscience". With this letter, I would like for us to explore the reasons for such a gap and to highlight the importance of building a bridge between these two concepts.

If it is rare to see evolutionary perspectives in a neuroscience article, it is not because the neuroscientific community rejects evolution, it is rather because it fails to consider it. Some of the guilt might still lie on the shoulders of anthropocentrism. Statements such as, "a trait conserved from mouse to human", are still in use and imply that mice are more primitive, which is why we rarely see the expression reversed (1). In the same vein, the term "model" has been overused, sometimes implying that rather than observing a biological process itself, we are observing the model of a human phenomenon in another species (2). In fact, most of our current research is based on what are, perhaps wrongly, referred to as "model species", with, amongst others, mice, zebra fish or drosophila. Accordingly, efforts to produce molecular and genetic tools have been heavily focused on these few model species. This choice has also been supported by the presence of conserved traits observed in both humans and the species of interest. For instance, genes such as FMR1 are conserved between mice and humans and seemingly support similar functions at both the molecular and behavioural scales (3). While this approach has been successful in many ways, it leads to two major issues. First, there is a conservation issue because "broadly conserved" traits have not necessarily remained functionally unchanged. For instance, humans and nematodes present a conserved gene which is respectively linked to Alzheimer's disease and to egg-laying (4). Drawing conclusions from the observation and manipulation of conserved traits can, thus, be tricky at times. The second issue concerns diversity, as a systematic study of conserved traits leaves aside a great deal of the Animal Kingdom's diversity. A

greater consideration of all animal species could participate in putting our research back into the context of their evolutionary histories, providing a potent tool to deflect the aforestated problematics.

For this purpose, combining comparative and experimental approaches offers an ideal framework for studying a neural process whilst taking into consideration its evolutionary path and its mechanistic causes. Accordingly, some researchers work with so-called "model clades". A clade is a group of organisms consisting of a common ancestor and all the species descending from that ancestor. In a model clade, the variation of a trait of interest is compared between the species included in the clade (5).

In a model clade one can study a conserved trait, such as a similar parenting behavior shared by the species. The behavior is either homologous, thus actually inherited from their common ancestor, or convergent, meaning that it evolved independently in some of the species (5). A key aspect of the conservation issue is that while homology is often the rationale for the observation of a specific trait in model species, it does not provide much information about the trait's function or importance (1). On the contrary, convergent traits, through their independent evolution, are thought to be important for the system. Convergent behaviors can have different underlying neural mechanisms, but they can also emerge from similar, converged, neural underpinnings. These can form a "mechanistic toolkit" providing a glimpse of the anatomical and physiological constraints under which the behavior has come to emerge independently in different species (5). For instance, Katz has been able to show in several species that neural circuits underlying rhythmic behaviors, dubbed central pattern generators (CPGs), present convergent membrane and synaptic properties. This toolkit is seemingly constrained by the necessity for a rhythmic output from the CPGs (6). Taken together, clues from converging traits can hint at generalizable principles of neuroscience – thus going further than the current, species-specific, conserved trait approach.

In his effort to uncover the general properties of CPGs, Katz studied both converging and diverging CPGs. While convergent CPGs have similar properties, divergent CPGs can present completely different cell populations, wiring and/or neuromodulation (6). The concept of "evolutionary divergence" translates into the natural variation and diversity observed between extant species; hence, this notion is key to address the diversity issue raised by the current model species approach in research. In fact, with evolutionary lenses, diverging traits in model clades give an opportunity to identify which upstream elements' alteration leads to the variation of the trait. From there on, it is possible to establish which characteristics are most likely to participate to the divergence, from a cell-type number to the connectivity of the brain area of interest (5). An evolutionary perspective allows the use of natural diversity to identify the key elements which explain why the nervous system of a species may be as it is and why it resembles some species' nervous systems, and not others. For instance, it was shown that the mutation of axonal guidance genes in several species with divergent motor patterns could completely rewire their CPGs and produce alternative motor patterns (6). The key role of axonal guidance in the production of different rhythmic activities suggests its importance for the evolution and diversification of CPGs. Conversely, it was also shown in a small model clade of two species, melibe and dendronotus, that CPGs with homologous neurons but different wiring were producing similar rhythmic behaviors. In this case, the divergent wirings seem to have undergone a "drift" which is inconsequential at the behavioral level (6). Studying divergent traits allow to take full advantage of the natural diversity of the Animal Kingdom. Moreover, they bring information about key pathways involved in the evolution of neural circuits and, when they do not affect the rest of the organism, they can highlight an underlying "drift" phenomenon.

Overall, the model clades comparative approach seems ideal for reconciling neuroscience and evolution. It promotes consideration and understanding of neural systems' evolutionary history using

the key concepts of convergence, divergence, and constraints; however, it should be noted that such methodology comes with its hardships. The choice of the model clade itself can be tricky and often involves trade-offs between statistical power, with larger numbers of species, and technical feasibility. In fact, some of our most powerful genetic tools are species specific (e.g. CRISPR). The model clades approach would therefore require further development of genetic toolkits to allow an optimal investigation of neural processes of interest in all the species involved. Importantly, if the model clade includes species which are separated by a large evolutionary distance (i.e. by more diverged traits), the comparison of neural processes underlying a trait of interest has more chances to be confounded (5). If the model clades approach has flaws, it still allows for insightful observations on the organisation and functions of nervous systems.

Neurons emerged in the last common ancestor to almost all multicellular animals more than 500 million years ago (4). To this day, comb jellies present uniquely fused neurons which would have evolved independently from the rest of multicellular animals (7). This other natural solution to neurotransmission provides an alternative understanding of nervous systems. There are many comb jellies species, thus, according to the model clades approach, we could comparatively study their fused neurons syncytia. We would be able to assess both their convergent and divergent properties. We might establish the general principles ruling these syncytia and the elements which determined their evolution in the stead of synapses. This, in my opinion, perfectly illustrates how we could strengthen our knowledge of our own nervous system by strolling along nature's diverse evolutionary paths; however, as the model clades approach will require many new resources, I will end this letter on possible first steps. Indeed, in 2013 Dehaene described the "recycling" of a visual area, from its ancestral role of encoding for faces and basic shapes, to its cross-cultural activation during reading. He managed to put the human nervous system back in the context of humans' evolutionary history with the emergence of reading 4000 years ago (8). Like him, other neuroscientists are starting to simply use known evolutionary history to contextualise their research (9,10). I am convinced that engaging with this change in mindset is key to further establishing an interdisciplinary bridge between neuroscience and evolutionary biology.

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Tender hands, heavy hearts: the unseen multifaceted struggles of caregivers. A focus on dementia

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This section has been created in collaboration with the Maison du Cerveau, an association that brings together all those involved with diseases from the nervous system. Our goal is to increase visibility and to provide information about these pathologies, treatments, and research advancements for the general public.

To my aunt and to my mother's care

She watches her sister, once vibrant and full of life, now a shadow of the woman she knew. As she gently brushes back her sister's hair with her fingertips, the conversation they once had, full of laughter as always, has been replaced by silence. A silence so profound that it speaks out loud about the fragility of memory and identity.

This non-fictive story shows how caring for a loved one with dementia is to embark on a journey where loss and love coexist. It is not merely the loss of memory but the gradual disappearance of a person's very essence, while the caregiver silently bears witness to both their decline and the evolution of their own identity.

What is dementia?

The diagnosis of dementia follows a set of criteria to distinguish it from other cognitive disorders. These include: **1)** evidence of cognitive and behavioral impairment through appropriate tests, **2)** a loss of autonomy (if autonomy is intact, it is considered as mild cognitive impairment), **3)** a noticeable change from the person's previous state, and **4)** the condition must be chronic, not acute, to exclude confusing syndromes.

Who are these silent pillars for their loved ones?

Always there to help, to care, to talk (even when there is nothing to say), to take the hands of those in need. There… in the shadow of medical institutions.

The caregivers of patients with dementia are for the vast majority women (from 70 to 80%) (1, 2, 3). Women are more likely to take on the role of primary caregiver, which is due to traditional gender roles and social expectations. Around 75% of them are family members of the patient (spouses, daughters, sisters, daughters-in-law, nieces, granddaughters), but they are sometimes friends (4). In the scientific literature they are referred to as "family caregivers" or "informal caregivers" to emphasize the unpaid

and untrained aspects of their work. It is also very important to point out that informal and family caregivers have not chosen to care for someone with a disease; they often stress that they feel obliged to take on this role (3). This makes them more vulnerable and subject to a psychological and emotional strain. Due to the advanced age of dementia patients (often more than 60 years old) the average age of family and informal caregivers is between 50 and 60 years old (usually adult children of the patient) but a substantial portion of these caregivers is more than 65 years old (usually spouses of the patient) (1). One-quarter of dementia caregivers are called the "sandwich generation" meaning that they care not only for an aging relative but also for at least one child (3). Most of the caregivers are working either full-time or part-time but caregiving responsibilities often force them to reduce working hours, take unpaid leave, or even leave the work environment entirely (5, 6, 7). Finally, most caregivers (around 60%) live with the dementia patient and the care is given at home (3).

It is important to point out that when a dementia patient receives no help from a family caregiver or an informal caregiver, this person lives alone. 8% of dementia patients are in this situation (3). These invisible caregivers are essential to the well-being and dignity of our elderly. It is then crucial to make their work visible.

What is their role? What does caring for someone with dementia really mean?

- Daily activities: household chores, shopping, preparing meals, providing transportation, arranging for doctor's appointments, managing finances and legal affairs, answering the phone, bathing, dressing, grooming, feeding, helping the person to walk, transfer from bed to chair, use of the toilet and manage incontinence (3, 4).

- Health and medication: helping the person to take medications correctly, either via reminders or direct administration of medications, helping the person adhering to treatment recommendations, very likely managing all the comorbidities of the patient, and more importantly providing emotional support (3).

- Symptoms coping: managing behavioural symptoms of dementia such as aggressive behaviour, wandering, depressive mood, agitation, anxiety, repetitive activity, and night-time disturbances (3).

- External support: finding and using support services such as support groups and adult day service programs, deciding for nursing home or assisted living care, hiring and supervising others who provide care, (3).

- Communication: addressing family issues related to caring for a relative with dementia, including communication with other family members about care plans, decision-making and arranging respite for the main caregiver (3).

What impact does caregiving have on caregivers? Do people that care for someone else care for themselves?

The experience of caregiving for patients with dementia has complex and multifaceted consequences because it requires total investment on the part of caregivers, a genuine self-sacrifice.

The health and well-being of caregivers are affected. Due to the tasks that they must cope with, their physical condition is greatly impaired (e.g. bathing, transferring from bed to chair), as is their psychological condition. Caregivers tend to have more musculoskeletal injuries, arthritis, hypertension, vascular diseases, and they often neglect their diet and physical activity (8). Moreover, the whole organization of the patient's life falls on the shoulders of the caregivers, and the resulting stress is immense. Caregivers are then more prone to anxiety, depression, and psychological distress than non-

caregivers. (3, 4). Certain factors are known to be linked to the consequences on health and well-being: being a woman accentuates distress, as their emotional investment is more pronounced than for male caregivers and they tend to spend more hours caring for the patient, being a family member, the quality of the relationship between the caregiver and the patient, satisfaction with life, and the level of self-esteem (4).

The social life is affected. Patients suffering from dementia require special care, which is often long, demanding and spread over several years. Under these conditions, caregivers tend to reduce their free time, their hobbies, the time they spend with friends and family, and the time they spend at work. As a result, over the years they feel more isolated and consequently receive less social support (3, 4).

The consequences are also financial, and mostly suffered by women since they constitute the majority of caregivers. Frequently, people taking care of someone else experience financial strain as they reduce their working hours, resulting in diminished income, retirement savings, and career advancement. Moreover, many caregivers, particularly women, shift to more flexible jobs to balance caregiving and employment. This trade-off often leads to lower job satisfaction and long-term financial consequences (5, 6). Another often overlooked aspect of dementia is the cost to caregivers. It includes medical consultations pharmaceuticals, provision of personal and nursing care, and often residential care in the later stages of the disease (4). It also includes small, variable, and unanticipated costs for caregivers, that can become substantial over years and years of caregiving.

All these consequences are known in the scientific literature as “caregiver burden” (9, 10, 11, 12, 13, 14), and although the concept is still a subject of debate (15, 16) it is important to mention that it is possible to cope with this burden and that some advice can be found (see Table 1) (17). Coping with this issue is crucial not only for the caregiver, but also for the patient. There is a strong positive correlation between the burden on caregivers and the deterioration of the patient's condition, which increases the risk of institutionalisation (18).

What is the specificity of the caregiver's experience for patients with dementia compared to other diseases?

Dementia is a long-term, progressive, and continuous deterioration in a person's psychological, emotional, and physical abilities, which means that caregiving responsibilities continuously increase over time. This trajectory places an emotional and psychological toll on caregivers, as they must constantly adjust to worsening symptoms and the loss of autonomy in their loved ones. As a result, the time spent caring for a person with dementia is much greater than for any other disease, and this time increases over the years (from 5 hours a day at the start of the disease to 10 hours after eight years) (3). The severity and type of symptoms contribute to the uniqueness of the care experience for caregivers of people with dementia. Dementia caregivers often face severe cognitive decline (e.g. memory loss), agitation, aggression, delusions, depression, anxiety, and resistiveness (19) or ‘resistance’ to care. This emotional toll is intensified as caregivers must navigate unpredictable behaviours that challenge their coping skills.

But the uniqueness of dementia, and by extension of its care, lies more in the gradual and insidious erosion of identity (20). The concept of identity is central in understanding both the experiences of dementia patients and their caregivers. As dementia progresses, the loss of cognitive functions leads to a loss of the personhood, autonomy, and agency. In these conditions, patients are unable to integrate the dimension of the self. Caregivers are witnesses to this loss; they have a front row seat to this erosion of identity. This creates an existential challenge in which they feel responsible for preserving the identity and narrative that the patient can no longer sustain on their own (21). In

addition, caregivers can experience a grief of identity. As a result, dementia patients die twice. The first occurs when their loved ones must mourn the loss of the person they once knew (20). This creates an emotional and existential burden: dementia patients are a cruel reflection of the finiteness of existence and the fragility of concepts of self and identity.

Dementia mirrors a change in the identity of caregivers: they were relatives, and then they became caregivers. They take now this role as their primary self-conception which alters the dynamic of the previous relationship. For adult child caregivers, this even leads to a reversal of care. They now have to care for their parent in the same way that the parent cared for them as a child.

Are the consequences of caring for someone with dementia only negative?

If the negative consequences of caring for a person with dementia are more pronounced, visible, and studied, it is necessary to seek out, examine and analyse the positive consequences. It will help medical professionals to support caregivers in their journey and caregivers to share their experience.

At the heart of every human being lies a driving force that enables us to overcome even the most difficult obstacles. That strength is known as resilience, and it is only possible through a quest for meaning. This quest for meaning is the ability to get something positive out of adversity, to make sense of any situation, and accept what has happened (22).

Caregivers can be motivated to undertake and persist with their role due to their past relationship with the patient. The caregiver's experience can be seen not only as a situation in which loss and love coexist, but also as one in which gratitude and hope coexist (23).

Three domains of positive outcomes have been identified by caregivers of patients with dementia (23).

Perceived benefits for the caregiver

- Personal growth and achievement: caregivers find themselves more patient and understanding; some learn that they need to enjoy their lives now rather than putting things off to the future; they learn new skills; some identify that the person with dementia trusts them and feels 'safe' with them.
- Glimpses of the person they used to be: some caregivers do not identify drastic changes in the patient's personality and recognise their role as maintaining the patient's identity. On the other hand, some caregivers identify changes but are able to recognise certain remaining aspects of the person (e.g. sense of humour).
- Making a difference: caregivers find satisfaction from knowing they can offer help, comfort, and support to the patient, by helping as much as they can and doing their best. Some can feel rewarded by the fact that the patient tells to other family members or friends what the caregiver did or sometimes just by receiving a smile from the patient.
- Accomplishing a duty: for some caregivers, being able to repay past help (such as adult caregivers that used to be the children of the patient) or fulfil marital vows is a positive element to providing care. Caregivers feel that the person with dementia would have done the same for them if they had needed care.

Perceived benefits for the person with dementia

- Helping to retain their independence: caregivers are satisfied that despite the diagnosis the patient with dementia can carry on as before and have a relatively 'normal life'. Some are keen to help the patient to live at home, surrounded by their loved ones and friends.

- Receiving good quality care: caregivers are concerned to maintain a safe environment for the patient and protect them from harm. Regarding to their long-standing relationship with the patient some caregivers believe that they best understand the patient's needs.

- They are happy and enjoying life: some caregivers identify that the patient's wellbeing is improved by their care. Witnessing a smile, a laugh or happiness is gratifying for them. It is important for caregivers to identify happiness and joy since they want to be sure that the patient lived a worthwhile and fulfilling life.

Perceived relational benefits

- A long-lasting relationship: Caregivers identify how their long-standing love for the person with dementia remains unchanged, that caregiving is a way of demonstrating their love and their shared history. Some describe how the patient still loves them. They insist on the fact that they are still together and do things together. Some have the feeling that they both support each other and manage the situation together. Others feel they have grown closer through caregiving, the patient being more affectionate towards them, and they think they know the patient better.

Caring for someone with dementia is a long and intense journey, and the resulting burden can be immense. Spouses, children, siblings, and friends do the unpaid, untrained, and sacrificial work of caring for people in need. They are there with all their love, affection, and help, taking the hands of people who do not remember what they were and sometimes do not see what they are now. They must cope with the multifaceted burden of caring, which encompass health, wellbeing, social and financial constraints. But maybe there is also the potential for strength, for love, and for a deep, enduring connection between the caregiver and the patient. It is then crucial to support caregivers not only through practical and emotional assistance but also by helping them recognize the positive aspects of their role. These moments of positivity are not just coping mechanisms; they are a testament to the resilience and strength of caregivers, offering a gleam of hope even in the darkest of times. The caregiver's journey is complex, but it also offers opportunities for profound emotional growth and, ultimately, healing.

Table 1. 10 important tips for caregivers to avoid burnout (adapted from Sullivan & Miller, 2015).	
Become educated about the disease	The more you know about the disease, the more empowered and the more comfortable you will feel with role changes. Ask as many questions as you need to when you are in appointments. There are no stupid questions. All of them are important.
Take care of yourself	As flight attendants say: "You must put on your own oxygen mask before putting on the mask of another." This philosophy applies to caregiving, too. If you are unhealthy emotionally or physically you will be of no help to anyone else.
Practice healthy living	You are much more capable of being of help to others when you eat a healthy, balanced diet, exercise regularly, are involved with your own interests and get enough sleep.
Stay social	Connecting with others in similar situations is powerful, because you no longer feel isolated, and you can learn from others. In addition, make sure you maintain other important relationships with children, family members and close friends.
Accept help	As difficult as it is to ask for help from others, realize that you need a break and that others may want to help. You do not have to do it all, nor is it healthy to do it all. The best way to avoid burnout is to accept help. People often want to be there for you: just ask.
Acknowledge your emotions	If you are feeling hopeless, worthless, helpless, sad, anxious, or fearful, acknowledge these emotions. These are all normal reactions to your situation.
Allow for healthy expression of your feelings with each other	Just because you are now a caregiver does not take away the fact that you had a relationship with this person in the past. You are still a spouse, partner, child, etc., and with that comes the responsibility to speak respectfully and openly. Should difficulties arise, seek couples or family counselling. Your multidisciplinary physician team will have a list of qualified mental health professionals.
Allow for caregiving holidays	This simply means taking some time away. You will be a better caregiver to your loved one if you do so.
Encourage healthy independence of your loved one	Help your loved one to be as independent as possible for as long as he or she can. This may involve assistive devices or new technologies.
Seek help through your local organizations	Each territory or state has its own society or organization dedicated to a specific disease. You can find these by typing "the National (insert disease) Association of (insert country)" in an Internet search engine.

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Women's Voices: Inspiring the Neuroscientist Community

Eduarda Gervini Zampieri Centeno

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Women's Voices is an interview section created in partnership with the Neurocampus Parity and Inclusion Committee (NeuroPIC) a local group committed to promoting equality and organizing actions to close the gap between women and men in academia. The goal of this section is to increase the visibility of early career female researchers at the Bordeaux Neurocampus of the University of Bordeaux. We interview researchers about their scientific contributions, insights and opinions about equity, diversity and gender bias in academia. Through these interviews, we aim not only to highlight their achievements but also to serve as inspiration for our scientific community and other female scientists.

Together, we will bridge the gap!

This month in Women's Voices we interview **Eduarda Gervini Zampieri Centeno**, a brazilian PhD student working in computational neurosciences and songbirds at the IMN. Eduarda is passionated for Open Sciences and programming in Python. Beyond her research at the University of Bordeaux, Eduarda dreams of launching a coding camp for girls in Brazil!

Sara Carracedo: Could you introduce yourself and give a brief background about your academic journey?

Eduarda Gervini: I come from the south of Brazil, where I began my scientific career with a BSc in Biotechnology. As an undergraduate, I had the opportunity to move abroad and spend a year as an exchange student at the University of Reading in the United Kingdom. Following my undergraduate studies, I joined the Neurasmus program (Erasmus Mundus program for Neuroscience), completing my first year at Université de Bordeaux and my second at Vrije Universiteit Amsterdam. After earning my master's degree, I returned to Bordeaux to start a PhD in Dr Leblois' team, while continuing to work remotely and part-time as a research assistant for the team where I conducted my master's thesis project under the supervision of Dr Douw and Dr Santos (MULTINET).

My academic and professional journey has been a constant 'going outside of my comfort zone' and embracing new challenges. I was initially trained in wet lab research and then, after five years and enough exposure to different techniques, I transitioned to computational and dry lab work. Nowadays, I am moving toward advocacy, leadership, and policy-making in Open Science, a movement I have been involved with since 2019.

Sara Carracedo: Which is your current research focus?

Eduarda Gervini: In my PhD project, I am developing a computational framework, inspired by the principles of Open Science, for managing and analyzing data in Dr Leblois' team at IMN. This framework is currently being used in various research projects, but my thesis focuses on uncovering the sleep-related neural dynamics that could underlie vocal learning consolidation in songbirds. Our team is dedicated to understanding how songbirds learn to sing, with the ultimate goal of applying these findings to gain deeper insights into how similar sensorimotor skills are learned across species.

In Amsterdam, I am responsible for implementing and supervising Open Science practices within Dr Douw's team and coordinating a working group for a departmental transition toward this framework. An exciting project we are currently working on is our 'Open Science Guidebook for Neuroscience', where we tailor Open Science implementations to the context of neuroscientific/biomedical research. Next to these tasks, I also participate in different Open Science-related boards at the national and international level.

Sara Carracedo: You have been deeply involved in the Open Science movement; could you tell us more about the initiative ReproducibiliTea you have created?

Eduarda Gervini: ReproducibiliTea is a grassroots initiative from the UK that brings people together to discuss improving research practices over a cup of tea. These journal clubs have spread worldwide, and I first encountered them during my master's in Amsterdam. A friend and I started the Vrije Universiteit ReproducibiliTea, hosting monthly sessions on Open Science in a safe, informal setting. This experience fostered a sense of community and deepened our understanding of research practices.

When I applied for my PhD in Bordeaux, I knew I wanted to continue with ReproducibiliTea. I pitched the idea to the Graduate Program, received their support, and in February 2021, we had our first BordeauxTea session. The first year was a success, and by the end, BordeauxTea became an ADUM-registered course, allowing PhD students to count it towards their training hours. In the second year, Fjola Hyseni joined me as a co-host, and we held ten sessions, including talks from guest speakers like a UNESCO Science Programme Specialist.

In its third year, BordeauxTea became the first Open Science workshop on the Neurocampus, with over 60 participants brainstorming research practices for a week. I have since stepped down, but the group is in great hands, and I'm excited to see how BordeauxTea evolves.

Sara Carracedo: As a woman in neuroscience, what is your opinion on gender bias in academia?

Eduarda Gervini: It is undeniable how present gender bias is in academia. Various fields, including Neuroscience, start with many more women in earlier career stages, but that does not translate into similar proportions at later stages of seniority, where (white cis) males remain as the majority. This 'scissor-shaped' reality is fairly well documented, and unfortunately, we also know that it's not only that – even in similar positions women can still earn less.

In my opinion, a lack of diversity is always a loss to the work environment and the broader research field. More diversity fosters creativity, which is essential for problem-solving. Additionally, a diverse group of researchers is likely to design projects with more varied and inclusive goals. In biomedical research, for example, diverse datasets from different populations can enhance the generalizability of findings and improve therapeutic solutions.

In any case, I think it is also important to think not only of gender bias but also other biases that intersect with gender, including race, ethnicity and sexual orientation. We should strive for a safer and more equal ground for everyone.

Sara Carracedo: As the Open Science manager in the MULTINETlab (VUMc – Amsterdam), what are your thoughts/advice about female leadership? Do you feel it is easier/harder than for men?

Eduarda Gervini: While some people may have a natural aptitude for leadership, most need training and ongoing evaluation to become good leaders. This is especially true in academia, where the focus is often on detail and project execution rather than managing and leading teams. Due to a structural lack of training, academics and researchers are typically not equipped with the necessary leadership skills, which can result in supervisors unprepared for their roles, leading to environments lacking support and effective management. Furthermore, there is a lack of two-way evaluation between supervisors and students which hinders the exchange of constructive and transparent feedback. This environment is challenging for everyone, but particularly for women, who face additional structural obstacles and are generally underrepresented in leadership positions. Leadership and management training should be a core part of research education at all levels, with a stronger incentive for women to participate. My advice is to find good mentors, community, and training to foster leadership skills. I was fortunate to have Drs. Douw and Santos as mentors. They noticed a leadership spark in me, actively worked with me to improve my skills, and provided space for me to grow. Their guidance allowed me to take risks and be bold in my aspirations.

Sara Carracedo: What advice would you give to young women aspiring to enter into a PhD program?

Eduarda Gervini: My main advice for starting a PhD is to ensure you will be in a safe and supportive environment. Talk to others about your potential team and assess if their work ethic aligns with your values. This is especially crucial for international students, as being abroad without a support network can be challenging.

Look for opportunities to build a community and support network that respects your cultural values and consider factors like access to familiar foods and a climate you're comfortable with—these can affect how "at home" you feel at the end of the day.

Finally, choose a project that genuinely interests you, and engage in extracurricular activities that bring you fulfilment and immediate rewards. The PhD journey can be lonely and slow to yield rewards, so it is essential to find daily sources of joy to sustain you through the ups and downs. For me, advocating for Open Science has been crucial in keeping me motivated and purposeful over the past four years. It brought me immense joy and rewarding moments, as well as a supportive community and valuable skills that I will carry with me for life.

Hahaha

Matthew M. Hurley

Juan García-Ruiz[1]
[1]Glia-neuron interactions team, Neurocentre Magendie, University of Bordeaux

What's neuronhub? It is an outreach website hosting interviews with researchers from all corners of the planet about their work in the field of neuroscience. The idea is that you get something from people who have a long career in science, that you learn something new and cool, and above all that you don't lose track of the latest discoveries in neuroscience that are being made in other parts of the world.

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What is Beethoven doing right now? De-composing.

Why do we laugh when we hear a joke? Why do we feel our brains tingle when we hear a pun? Sometimes a short statement like Beethoven's is enough to make us laugh. We feel a sense of reward when we discover that decomposing could refer to body decay or to the antonym of composing music. But humor is more than puns.

An English, a French and a Spanish researcher meet in a bar after a congress and the Spanish researcher tells the others: good evening gentlemen, what are you going to drink?

Sometimes humor is constructed from meanings or circumstances shared by a group of people or a community, like the Spanish researchers' community, which is united by the precariousness of academia in their country. This type of humor not only increases cohesion among these people, but it is an elegant and funny way to make a social critique. And this is just one more example. Humor is difficult to define because it has no limits. But the intriguing thing is that we are one of the only species that laugh, at least that we know of. And we laugh at everything, even at our own downfalls. Humor is a mystery.

Matthew is a theorist, interested in biology and cognition. He turned his dissertation on the emotions that drive cognition into the book Inside Jokes, along with his coauthors, Daniel Dennett and Reginald Adams. He is now working towards understanding how goal-directedness comes to exist.

Juan García Ruiz: What led you to study laughter?

Matthew M. Hurley: I first became aware that we ought to theorize about humor when a friend of mine, the late Sasha Chislenko, shared his own theory of humor with me. And as I thought about it over the next couple years, I realized the topic was more important than we normally imagine it could be. The idea that we enjoy humorous stimuli, that somewhere and somehow in our biological and psychological constitution there exists an emotion that is devoted to this category of perception, means it most likely is very important to the kind of existence that we live. But the fact that we usually laugh at someone's failings, even if it is our own, made me wonder what it could be about failing that we should enjoy. When I then took a class in humor theory, taught by Reg Adams, I was given the opportunity to try to answer the question, and Inside Jokes is the result of further developing that answer.

JGR: Why do we enjoy puns? Do we enjoy them for the same reason we enjoy seeing someone falling down?

MMH: I think puns may just be one, somewhat accidental, source of humor. I'm glad you used the term enjoy here, instead of laugh at. We don't just laugh at things, when something is truly mirthful we enjoy it deeply and feel quite rewarded by it. Enjoyment forms the core of my work: the epistemic emotion theory. The main idea of it is that we have a series of emotions (including confusion, doubt, and curiosity) that serve epistemic functions. In other words, these emotions teach us the cognitive behaviors that constitute thinking. The epistemic emotions teach us to look for information, to root out contradictions, and generally to curate our knowledge of the world. We feel a distinctive type of ache when things are contradictory, and another sort of discomfort when the pieces of a puzzle just don't fit. There is a kind of mental hunger that compels us to figure out how things work. We get a unique shiver in our spine when we do discover some unifying clarity while contemplating a project. Mirth, I propose, is the special kind of delight that rewards us for discovering that we have leapt to a conclusion. The emotion is there in order to encourage us to do more of the kinds of thinking work that we just did to discover the mistake.

Most puns tend to take advantage of this system simply by setting up situations that are likely to cause us to make interpretive mistakes about the meanings of words as they are being said or read. As we first come across a pun, our minds jump first to the conclusion that the words have one meaning (Two goldfish are in their tank), and then discover that we've been led down the garden path, so to speak, as we realize there is a more fitting meaning, given the rest of the speaker's phrase or sentence (One of them says to the other, "you man the guns, I'll drive"). The comedian here got us to jump to the conclusion that the fish are in a fish tank, and it turns out it was a military tank. But it's not a great joke. The punster sort of rough-handled us to make that happen, so we may be a little amused, but possibly a little annoyed at the same time.

JGR: What is the essence of humor?

MMH: This time, I'm thrilled that you used the word essence. Although my theory sounds somewhat essentialist, I believe it best not to think of a thing such as humor as having an essence at all. Mirth interacts richly with the remainder of the contents of our minds, sometimes being enhanced and other times being canceled. The category of humor stimuli then becomes a richly evolving landscape.

To try to give a bit of detail about this idea, we might notice first that, while humor's main purpose is to discover natural moments in our everyday lives, jokes nonetheless become manufactured, unnatural things that are evolved and shared precisely in order to make one another feel amused. They become a kind of candy for the mind. Comedians might add in, or emphasize, a bit of surprise or wonder in their stories. Sometimes jokesters throw in a little taboo breaking, or they add some sexual innuendo that delights the mind in still other ways.

There is this game in our culture of trying to entertain one another by taking advantage of reward systems that were meant to serve other purposes, and while the enjoyment of this game may not necessarily all be mirth, still, because these types of enjoyment often or usually come packaged together with mirth, we tend to consider a large number of these things to be jokes. As you can see, this makes it very hard to simply give an essence.

JGR: Jokes are related to some extent to mistakes, and we enjoy those mistakes. Do we learn from them?

MMH: Great question. We don't necessarily need to learn from the mistake, although in some cases it may be quite beneficial. In the case of the goldfish pun, we don't need to teach ourselves a lesson such as "it is better to be open-minded to the fact that tank in the context of fish might mean something other than fish-tank". That would be a terrible lesson. Many of our first impressions, the conclusions we leap to, are the ones we would want to leap to. We draw those conclusions because they are the most likely interpretations. And that skill, in itself, serves us well in the bulk of our reasoning. What I suggest we actually learn from humor is the habit of thinking carefully, and double-checking things in our minds. The reward teaches us to be vigilant thinkers, and this helps us to reduce mistakes in the future and to generally curate our knowledge more cleanly.

JGR: Some people enjoy very stupid jokes while other people enjoy more elaborated humor. Is humor related to intelligence in some way?

MMH: I enjoy stupid humor among other kinds. I love watching people take falls, or even taking them myself. I giggle often about the simplest of stupidities in my everyday life. These kinds of things are often extra funny, in my opinion, because the confidence we have that we won't make such mistakes is undermined by the fact that we actually make them.

Humor is definitely related to intelligence. As I've described it, it appears to be a factor that helps create and sustain the very kind of intelligence that we have. But there doesn't seem to be a simple connection between how intellectual joke is, and how intelligent a person who enjoys it may be. Perhaps part of the reason is, as I pointed out before, that a well-developed joke potentially gives the audience many things to enjoy, not just mirth. And there is no accounting for taste, is there?

JGR: Do you know about labs focusing their research on humor?

MMH: There are a number of labs these days that are working in various ways on humor, and a few that focus solely on the topic. Some scientists have made a career of it. There are some people studying humor theories at the high level, attempting to adjudicate between theories based on whether people laugh at certain kinds of stimuli or not. And there are some labs looking for neural correlates of humor through fMRI, for instance. However, I tend not to keep a close pulse on this kind of work in general.

JGR: Is humor only human?

MMH: Those who have worked with great apes have reported getting the distinct sense that those creatures have some level of mirthfulness. Perhaps the trait exists in an even broader variety of animals. Laughter-like behaviors have been documented in other species like penguins. I don't find it convincing that a species so different from us as penguins necessarily has true internal mirthfulness. Nor that it has the need to communicate that mirthfulness, nor that any such communication ought to be a signal that sounds anything like our own. I find it much more likely that what is called penguin laughter is more loosely akin to a cat's purring than it is to our own laughter.

The trait ought to have evolutionary value to any animal that does a lot of thinking. But a possible trait's potentially having value doesn't mean that evolution has yet discovered how to give that trait to that animal. The major stumbling block in knowing whether other species have humor is that we can't directly access or talk

about those species' feelings. We can try to experiment with non-verbal situations that we find humorous, and see if they get some unusual reaction from the other animals as well, but still it will be hard to tell if that reaction is tied to mirth, surprise, confusion, or some other kind of perception.

JGR: If you take a human after birth, put it in a human-size box far from other human beings and you observe him or her for years, do you think you will ever see traces of humor? In other words, does humor need to be social? Does it depend on language?

MMH: Another excellent yet hard to answer question. I've wondered this too. In fact, when writing Inside Jokes, I think I took, a little too strongly, the position that evolution had built the trait directly. At this point, I still think that that might be possible, but I am much more open to the alternative idea that evolution built a more general emotional system that has the ability to be guided by culture in learning to attach value to specific categories of content. In my opinion, that subject itself is an important avenue for future research in trying to understand how our minds and any minds might operate.

JGR: What is Inside jokes?

MMH: My way of seeing Inside Jokes is that it uses humor as a central example in the exploration of the more general notion that our processes of thinking are directed by our emotions. It explores the thesis that reasoning itself, often seen as the antithesis of emotion, is in fact a result of emotion. And it makes the case that, if we hope to understand and perhaps one day construct something that is like us, in the sense of, say, being intelligent enough to discuss one's own place in the universe and so on, then that something will likely need to be built from the ground up as an emotional machine.

JGR: What exactly are you studying right now?

MMH: I intended for a while to study the processes of creativity and, in more detail, how the epistemic emotions might encourage creative thinking processes, and I held a particular interest in determining how we might build computational models of these processes. However, I became stymied in approaching that work by the deeper questions of, if we are to build artificial intelligence machines, what, or rather whose, goals will that creative intelligence serve?

So I shifted gears, roughly ten years ago now, and began to study the abstract and subjective notion of goal-directedness. What it is, and how it comes to arise, in an objective world. I hope to publish my work on this topic soon.

JGR: Do you have a general message you would like to share with the readers?

MMH: I think if any readers are interested in the topic of artificial intelligence, they've probably read tons of things about neural networks and machine learning. Maybe old-fashioned AI projects that involve search processes. Now is not the time to argue in detail for an alternative, but I want to tell the reader that there exists someone out here, who takes a fairly serious interest in artificial intelligence at the theory level, and yet who thinks that very little, if any, of the topics being studied in the modern field truly matter to understanding the subject.

For more interviews, visit www.neuronhub.org

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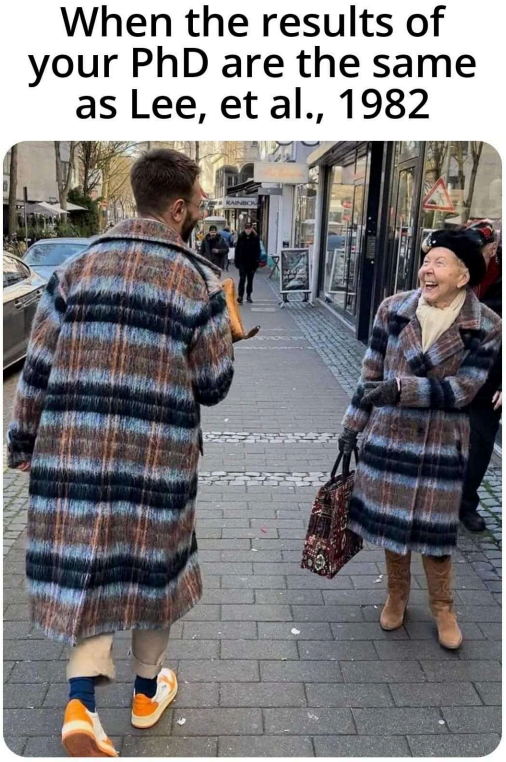


Simon Lecomte, 4th year PhD student at the IINS

Announcements

Award: Best Review Article of the Year

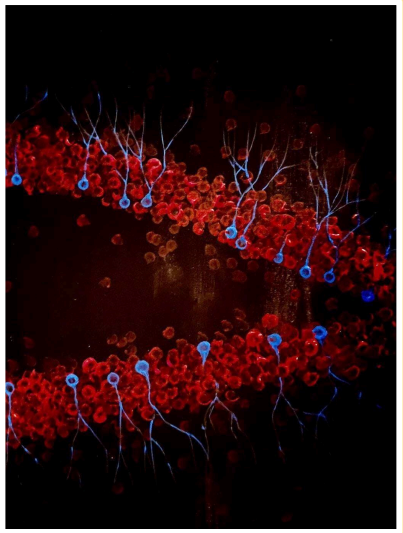
Title: The life of an engram
Author: Flávia Viegas Simões
Published in Brainstorm: 10th Issue (July 2024)

We are thrilled to announce that Flávia Viegas has been the selected winner of the "Best Review Article of 2023-2024" award, a recognition that comes with a cash prize of 100 Euros!

This award celebrates the exceptional contribution of our authors to the field of neuroscience through their insightful review articles. The winning article was selected by the editors based on its originality, literacy, and its relevance to the neuroscience community.

Warmest congratulations to our winning author!

Award: Best Cover of the Year



Title: Dentate gyrus of the hippocampus
Author: Vasika Venugopal
Published in Brainstorm: 8th Issue (February 2024)

For the first time, the Brainstorm Student Journal is thrilled to announce the "Best Cover of 2023-2024" award. Vasika Venugopal has been the selected winner with their acrylic painting entitled "Dentate gyrus of the hippocampus". This award comes with a cash prize of 100 Euros!

This award acknowledge the work of the artist behind the issue's cover. Their effort connects neuroscience research with the beauty of art.

Warmest congratulations to our winning illustrator!

Formations

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PhD seminar series

The PhD seminar series this year will focus on alumni from the Neurocampus. Do not forget to register your participation on ADUM for the 1st semester. Deadline on 27th October 2024.

Editorial board

Ludovica Congiu

Hailing from Sardinia (Italy), Ludovica obtained a master's degree in Neuropsychobiology at the University of Cagliari and pursued a Ph.D. in neuroscience at the Universitätsklinikum Hamburg-Eppendorf (UKE) in Hamburg. Currently, she is a PostDoc at the IMN, where she is investigating the role of P2X4 receptors in ALS and anxiety disorders.

Khadija Inam

Khadija is a Clinical Research Associate in Centre Hospitalier Charles Perrens. With a Bachelor's degree in Applied Biosciences from the National University of Sciences and Technology, Pakistan, and a Master's degree in Neurosciences from the University of Bordeaux, she has seamlessly transitioned from the academic corridors to the clinical trials. Her expertise is mainly focused on neuropsychiatric disorders.

Sara Carracedo

Born in Spain, Sara is a PhD student at the Neurodegénératives Diseases Institute (IMN). She holds a Veterinary Medicine Bachelor's degree from the University of Santiago de Compostela and the NeuroBIM Master's degree from the University of Bordeaux. Her PhD is focused on understanding the microglial and neuronal role of P2X4 receptor in ALS.

Toshiko Sekijima

Toshiko, originally from New Zealand, is currently PhD student at the Nutrition et Neurobiologie Intégrative (Nutrineuro). She holds a bachelor's in Biology from the University of Hawaii and a master's in agro-biomedical Science from the University of Tsukuba, Japan. She is also passionate by scientific illustration!

Juan García-Ruiz

With two Bachelor's degree, in Psychology and Biochemistry, and the NeuroBIM Master's degree from the University of Bordeaux, Juan is pursuing a PhD focused on the role of lactate in basal synaptic transmission. Although he speaks near-perfect French, Juan comes from Huelva, Spain. He is also the co-founder of neuronhub (www.neuronhub.org).

Simon Lecomte

Simon is originally from Lyon, France. He did his Bachelor's of Psychology from Strasbourg, after which he did the NeroBIM master's degree from the University of Bordeaux. He is a PhD student in the IINS where he is studying how the Fragile X Syndrome impacts the presynaptic mechanisms at the DG-CA3 synapses.

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You can write either a short-review on a topic of your choice, a one-page letter (a reflection, a project or an insight you would like to share) or a neurojoke.

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