16th Issue, October 2025

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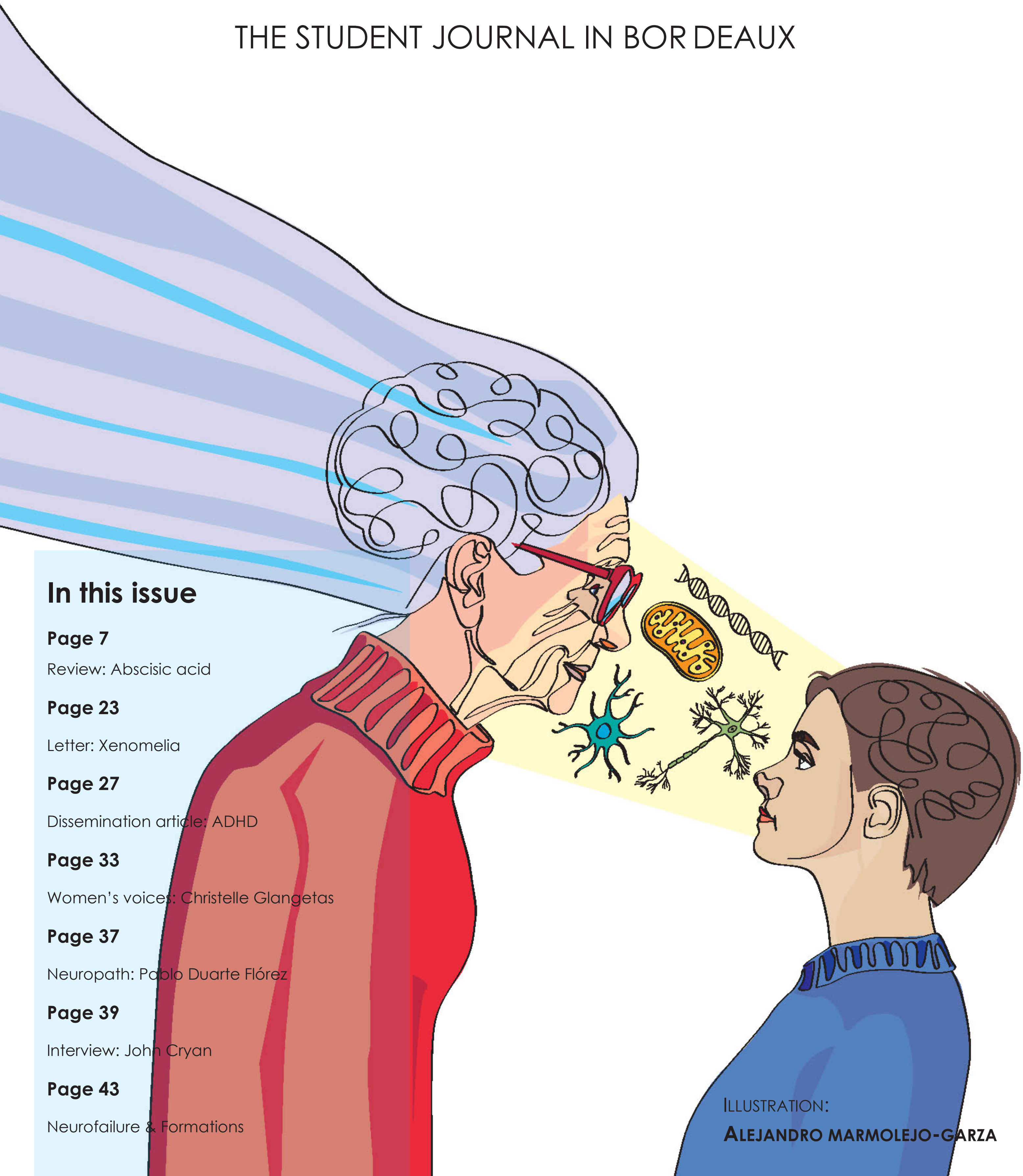
THE STUDENT JOURNAL IN BORDEAUX



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This journal received funding from the EURE-0028 project

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Abscisic acid, an evolutionarily conserved hormone: Therapeutic and diagnostic applications in mammals

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Received: 19th September, 2025 I Peer Reviewed: 29th October, 2025 I Accepted: 3rd October, 2025

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Abstract

Abscisic acid (ABA), a phytohormone known for plant stress responses, also plays key roles in mammalian defense mechanisms. Mammalian cells synthesize ABA during health challenges, influencing inflammation, insulin signaling, and disease outcomes via receptors such as PPAR-γ and LANCL-2. Research highlights ABA's therapeutic potential in neurological disorders, cancer, malaria, and other conditions linked to inflammation. Studies suggest ABA levels may serve as biomarkers for disease progression and treatment response. This review summarizes current knowledge of ABA signaling pathways and preclinical findings, while emphasizing the need for a deeper understanding of its metabolism and validation through clinical trials.

Keywords

Mammalian hormone, Therapeutic applications, Biomarker tool, Immune modulation, Animal model, Neurological disorders

Abbreviations

6-OHDA – 6-hydroxydopamine
Aβ – Amyloid β protein
ABA – Abscisic acid
ACC – Anterior cingulate cortex
AD – Alzheimer's disease
AMPK – AMP-activated protein kinase
APE-1 – Apurinic/apyrimidinic endonuclease 1
APP – Amyloid-beta precursor protein
ARDS – Acute respiratory distress syndrome
ATP – Adenosine triphosphate
BAT – Brown adipose tissue
BDNF – Brain-derived neurotrophic factor
cADPR – Cyclic adenosine diphosphate-ribose
cAMP – Cyclic adenosine monophosphate
COPD – Chronic obstructive pulmonary disease
COX2 – Cyclooxygenase 2
CRABP2 – cellular retinoic acid binding protein 2
CRH – Corticotropin-releasing hormone
DIO – Diet-induced obese
ER – Endoplasmic reticulum
ERK – Extracellular signal-regulated kinase
FABP5 – Fatty acid binding protein 5
FST – Forced swim test
GLUT-4 – Glucose transporter type 4
GRP78 – Glucose-regulated protein 78
HFD – High fat diet
hiPSCs – Human induced pluripotent stem cells
HPCs – Hematopoietic progenitor cells
HSP70 – Heat shock protein 70
icv – Intracerebro-ventricular
ip – Intraperitoneal
IR – Insulin receptor
IRS1 – Insulin receptor substrate 1
IRS2 – Insulin receptor substrate 2
JNK – Jun N-terminal kinase
LANCL-1 – Lanthionine synthetase C-like 1
LANCL-2 – Lanthionine synthetase C-like 2
LPS – Lipopolysaccharides
LTP – Long-term potentiation
MAPK – Mitogen-activated protein kinases
MCP-1 – Monocyte chemoattractant protein-1
MMP-9 – Metalloprotease-9
MSCs – Mesenchymal stem cells
NF-kB – Nuclear factor kappa B
NO – Nitric oxide
PCa – Prostate cancer
PD – Parkinson's disease
PGC-1 – Peroxisome proliferator-activated receptor-gamma coactivator
PGE2 – Prostaglandin E2
PI3K – Phosphoinositide 3-kinase
pIC – Posterior insular cortex
PKA – Protein kinase A
PKC – Protein kinase C
PPAR-γ – Peroxisome proliferator-activated receptor gamma
PPAR-β/δ – Peroxisome proliferator-activated receptor beta/delta
RA – Retinoic acid
RAR – Retinoic acid receptor
ROS – Reactive oxygen species
SIRT1 – Silent information regulator 1
STZ – Streptozotocin
T2R – Type 2 taste receptor
TNFα – Tumor necrosis factor alpha
VSMCs – Vascular smooth muscle cells
WAT – White adipose tissue

Introduction

In the mid-20th century, the first molecular complex regulating plant growth was identified as an acidic compound that inhibited the development of potato plants [1]. A few years later, acidic molecules responsible for abscission (shedding) were isolated from cotton fruits and were named abscisin I and abscisin II [2]. With time, abscisin II was renamed as Abscisic acid (ABA) [3]. Extensive research soon revealed that ABA is a key phytohormone that regulates plant growth, senescence, and abscission in response to stressors such as low temperatures, drought, nutrient deficiencies, and excessive UV irradiation (for review, see [4,5]).

Le Page-Degivry et al. published in 1986 the presence of potentially endogenous ABA in mammal tissue. In this study, cis-ABA and ABA-conjugated glucosides and ethers (similar to those in plants) were detected in pig tissues, including the brain, kidney, and heart. Now, almost forty years later, accumulating evidence confirms that ABA is synthesized in mammalian organisms, with important implications in mammalian pathophysiology. ABA is now recognized as a unique example of an evolutionarily conserved hormone that triggers defense mechanisms in response to stress. Given ABA's ability to activate defense signaling pathways, growing evidence supports its potential as a treatment and even as a biomarker of disease.

Methods

The compilation of articles cited in this review has been found through PubMed, using the following keywords: abscisic acid, mammalian hormone, neuroinflammation, oxidative stress, stress response, receptors, signaling pathways, animal models, therapeutic applications, biomarker, and neurological disorders.

An extended version of this review can be found in: Gharib A, Marquez C, Meseguer-Beltran M, Sanchez-Sarasua S, Sanchez-Perez AM. Abscisic acid, an evolutionary conserved hormone: Biosynthesis, therapeutic and diagnostic applications in mammals. Biochem Pharmacol. 2024;229:116521.DOI:10.1016/j.bcp.2024.116521.

Results and discussion

ABA mammalian receptors

Various studies have identified Lanthionine synthetase C-like 2 (**LANCL-2**) as the mammalian receptor for ABA [6,7]. LANCL-2, widely expressed with LANCL-1, is a key immune and metabolic regulator, and its agonists show therapeutic potential in inflammatory diseases [8].

ABA can also activate the peroxisome proliferator-activated receptor gamma (**PPAR-γ**), a transcription factor controlling adipogenesis, insulin sensitivity, and glucose homeostasis, making it a target for treating inflammation-related disorders [9–11].

Beyond these, ABA antagonizes the bitter taste receptor 'type 2 taste receptor 4' (**T2R4)**, resulting in reduced intracellular Ca2+ levels [12]. T2 receptors are not unique to oral tissue, and they have been found expressed in the nervous system [13]; airway muscle cells [14], heart, and gastrointestinal tract [15]. This suggests roles of ABA in taste modulation and broader physiological functions [12].

Additionally, ABA influences apoptosis via the retinoic acid receptor (**RAR**) pathway and binds the heat shock protein 70 (HSP70) and the glucose-regulated protein 78 (GRP78), which regulate endoplasmic reticulum (ER) stress and glucose metabolism, highlighting potential novel therapeutic mechanisms [16–18].

Collectively, these actions allow ABA to modulate the expression of cytokines and other factors, providing protection, inflammatory response and/or differentiation and apoptosis. It is important to note that knowledge is still incomplete, like ABA metabolism, degradation and/or export.

Effect of ABA on mammalian cultured cells. Mechanism of action

Scarfi and colleagues [19,20] demonstrated that exogenous ABA significantly influences mesenchymal stem cells (MSCs) and hematopoietic progenitor cells (HPCs) by promoting in vitro expansion, migration, and proliferation through cyclic adenosine diphosphate ribose (cADPR) and calcium signaling (Fig. 1). Blocking ABA with an antibody showed that micromolar concentrations triggered nuclear factor kappa B (NF-kB) nuclear translocation, stimulating CD34+ stromal and endothelial cells growth; thus, suggesting both autocrine and paracrine effects.

ABA also promotes human induced pluripotent stem cells (hiPSCs) maturation into HPCs and megakaryocytes (platelet precursors) via protein kinase A (PKA), cADPR, and mitogen-activated extracellular signal-regulated kinase (ERK) 1/2, highlighting potential applications in thrombocytopenia [21,22].

Initially, ABA was considered pro-inflammatory. It was shown to stimulate monocyte migration by increasing NF-kB translocation, leading to augmented cyclooxygenase-2 (COX2), prostaglandin E2 (PGE2), monocyte chemoattractant protein-1 (MCP-1), and metalloprotease-9 (MMP-9) levels. Since atherosclerosis is driven by the migration of vascular smooth muscle cells (VSMCs) at endothelial lesions, ABA was concluded to play a pro-inflammatory role in atherogenesis [23]. Granulocytes exposed to ABA showed enhanced chemotaxis and reactive oxygen species (ROS) production, while microglial cells increased migration toward amyloid-beta (Aβ), producing nitric oxide (NO) and tumor necrosis factor-alpha (TNFα) (Fig. 1) [24]. However, other studies demonstrated anti-inflammatory effects, with ABA reducing LPS-induced cytokines expression and oxidative stress in murine macrophages [25]. These results indicate that ABA can both promote and resolve inflammation depending on timing and context.

Beyond immune regulation, ABA enhances glucose metabolism. At low concentrations, it stimulates insulin release from pancreatic cells, while higher concentrations trigger secretion without glucose, suggesting an autocrine role [26]. In adipose and muscle cells, ABA improves insulin sensitivity by upregulating glucose transporter type 4 (GLUT-4), promoting glucose uptake, oxygen consumption, and adiponectin and brown adipose tissue (BAT) gene expression [27]. In muscle cells, ABA activates the AMPK/PGC-1α/SIRT1 pathway, enhancing glucose transport and mitochondrial respiration [28]. Interestingly, when LANCL-2 was knocked out in these cells, LANCL-1 was overexpressed and could mediate ABA's effects, improving glycemic response to glucose load [28]. This suggests that LANCL-1 may also serve as a potential ABA receptor.

In cardiomyocytes, ABA improves mitochondrial function and NO production. Furthermore, in human myotubes, it boosts ATP generation, glycogen synthesis, and muscle performance [29,30].

At higher concentrations, ABA shows pro-apoptotic effects on cancer cells. In leukemia and glioblastoma cells, it reduced viability, induced apoptosis, and modulated retinoic acid pathways by increasing cellular retinoic acid binding protein 2 (CRABP2) and decreasing fatty acid binding protein 5 (FABP5), likely through RAR-α [16,31,32]. Further studies linked its effects to autophagic activation via mitogen-activated protein kinases (MAPK)/Jun N-terminal kinase (JNK) signaling [33]. In prostate cancer, ABA induced G0 arrest through LANCL-2 and PPAR-γ, activating p38MAPK signaling (Fig. 1) [34,35].

Finally, in neuroblastoma cells, ABA reduced corticotropin-releasing hormone (CRH) mRNA expression by upregulating RAR-α [36].

Together, these findings indicate that ABA is involved in many different processes through multiple receptor-mediated signaling pathways.

Therapeutic ABA applications. Evidence from animal models of human disease

ABA has been tested in a wide range of preclinical models, and its beneficial impact is increasingly recognized. Herein, in Table 1, we provide a shortened review of ABA's impact and the mechanisms underlying its potential therapeutic effect (for a complete version of Table 1, please see [37]).

ABA as a biomarker, a potential new tool to help in diagnoses

Evidence suggests that optimal ABA concentrations protect against disease, supporting its potential as a biomarker. Patients with chronic obstructive pulmonary disease (COPD), asthma, and acute respiratory distress syndrome (ARDS) showed significantly reduced ABA levels compared to healthy controls, together with lower LANCL-2 and PPAR-γ expression and correlations linking ABA to immune regulation and reduced inflammation [38–40].

In glioma tissue derived from patients, ABA correlated positively with CRABP2 and negatively with FABP5, indicating a role in apoptosis and tumor suppression [16]. Paradoxically, high-grade gliomas (stages III and IV) exhibited lower ABA levels, possibly due to depletion of cellular ABA resources after chronic inflammatory stimulation, similar to cortisol exhaustion under prolonged stress [41]. These findings highlight ABA's diagnostic potential and open a new avenue of research to unveil the pathophysiology of ABA in mammals.

Conclusions

Traditionally recognized as a plant hormone, accumulated evidence supports ABA as a universal signaling molecule with hormone-like properties and an essential role in survival mechanisms.

Although the biosynthetic pathway in mammals is not yet completely elucidated, apparently newly synthesized ABA is released by mammalian cultured cells in response to specific danger-like stimuli, supporting its role in activating defense mechanisms. Once released, ABA functions through autocrine, paracrine, and endocrine mechanisms, influencing numerous biological processes.

Current evidence suggests that ABA uses ionic transporters to enter cells. Inside the cell, several intracellular receptors have been shown to bind and mediate ABA effects. The most studied receptors, PPAR-γ and LANCL-2, are ubiquitously expressed across various organs and tissues, indicating a widespread role in mammalian functioning. Also, computational modeling is expanding the list of potential ABA receptors, highlighting ABA's role in fine-tuning mammalian physiology.

The extensive literature reviewed highlights the potential therapeutic applications of ABA administration in a wide range of animal models of human disease. Emerging evidence also suggests that ABA levels measured in biofluids or tissue samples may serve as biomarkers of human disease. ABA's properties suggest an interesting parallel with cortisol, another hormone released in response to stress with receptors ubiquitously expressed throughout the body and a significant impact on overall physiology.

Like cortisol, which is used as a potent anti-inflammatory medication and a biomarker of inflammation, ABA could have evolved similarly. A notable difference is that ABA is synthesized by different cell types across various organs, including immune cells, whereas cortisol is mainly secreted by the adrenal glands. We proposed that when ABA-mediated defense is insufficient, symptoms appear, and exogenous ABA administration may improve disease outcomes. This is supported by human studies where high ABA levels correlate with better prognoses and can be used as biomarkers of disease status.

Despite the additional research required to elucidate ABA's pathophysiology, therapeutic value, biosynthesis, cell release pathway, and metabolism in mammals, the literature reviewed clearly indicates that ABA is gaining recognition as a molecule with significant potential in research and clinical applications in humans.

Did you know?

In the USA, since 2010, ABA has been commercialized as a dietary supplement for glycemic control by the enterprise *Biotherapeutics Inc.*

In 2017, *Euromed SA* reached a license agreement with *Biotherapeutics Inc.* for patented technology for ABA, leading to launch ‘ABALife™’ in Europe.

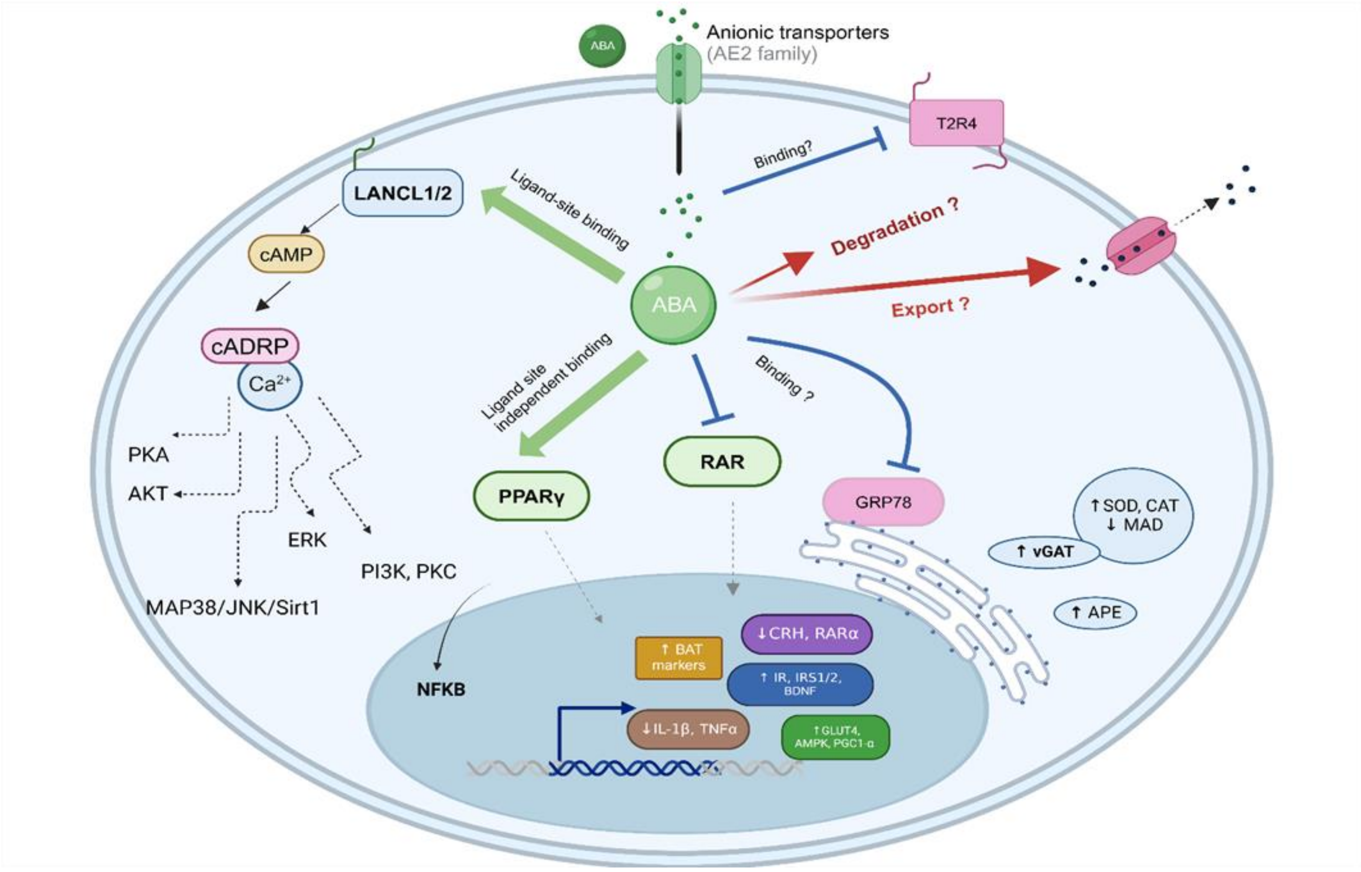

Fig.1. Potential mechanism of ABA Action in mammalian cells. ABA has been reported to enter mammalian cells via anionic transporters, though its complete life cycle within the cell remains unclear. The mechanisms of ABA secretion or export are not yet understood. Several receptors for ABA have been identified, with LANCL2 being the primary mediator, though LANCL-1 can also bind ABA in certain cell types. PPAR-γ is another significant mediator; ABA can bind to PPAR-γ in a ligand site-independent manner and has been shown to increase PPAR-γ activity and/or expression in some models. Additionally, ABA has been reported to interact with the RAR and the endoplasmic reticulum protein GRP78, although the precise binding sites are unknown. Only one antagonistic action has been reported on the taste receptor T2R4. Further research is warranted to fully understand this action. Activation of LANCL-1/2 by ABA leads to increased intracellular calcium levels, which can activate various signaling pathways depending on the cell type and environmental conditions. Reported pathways include PKA, AKT, ERK, and the p38MAPK/JNK pathway, which subsequently leads to SIRT1 activation. ABA can also induce the activation of NF-κB, resulting in its translocation to the nucleus. Collectively, these actions allow ABA to modulate the expression of cytokines and other factors, leading to either a reduction in proinflammatory cytokines or an increase in trophic factors. It is important to note that not all pathways may be involved in every cell type; this figure aims to summarize most of the known pathways and highlight areas where knowledge is still incomplete, like degradation and/or export. Through these mechanisms, ABA can act upon different cell types, providing protection, inflammatory response and/or differentiation and apoptosis.

Table 1. **Exogenous ABA administration *in vivo*.** Potential therapeutic effect demonstrated in animal models of disease.

		ABA treatment				
Disease	Animal model	Dose	Duration	Effect	Via	Ref
Cancer	PCa xenograft in mice	20 mg/kg i.p.	Twice daily for 8 weeks	• Induction of dormancy state of PCa cells in the bone marrow microenvironment		[34]
	UG87MG xenograft mice	60 mg/kg i.p.	Once daily for 21 days	• Reduce tumour size; increase autophagy markers	MAPK/JNK signaling	[33]
	Albino male rats	100µg/ml	1 time (*ex vivo*)	• Prevention of angiogenesis with and without prednisolone		[42]
Metabolic syndrome	db/db mice fed with HFD	100 mg/kg (dietary administration)	36 days	• Reduction of blood glucose concentrations • Improvement of adipocyte hypertrophy, TNFα expression, and macrophage infiltration in WAT	PPARγ and cAMP/PKA signaling pathways	[43–45]
	DIO mice	0.125µg orally	Daily for 12 weeks	• Improvement of glucose tolerance and insulin sensitivity • Increment of glycogen synthase, fatty acid oxidation markers, glucose oxidation markers and mitochondrial metabolism genes	LANCL-2	[30]
	HFD rat model	20 mg/L in drinking water	12 weeks	• Amelioration of peripheral insulin resistance • Improvement of cognitive performance • Reduction of microglia activation and TNFα mRNA levels in the hypothalamus • Restoration of IRS1, IRS2, TNFα, BDNF and APP levels and alterations in neurogenesis in hippocampus		[46,47]
	STZ-induced diabetes rat model	Central 10-20 µg i.c.v	14 days	• Improvement of learning and memory alterations • Ameliorative effect on LTP induction in CA1 layer	PPAR-β/δ, PKA	[48,49]
	STZ-induced diabetes mouse model	5 µg/Kg orally (single dose) or in drinking water	Single dose or 4 weeks	• Reduction glycemia profile (single oral dose) • Increase insulin sensitivity in skeletal muscle	AMPK, PGC-1, IR, GLUT-4	[50]
Alzheimer's disease	3 x Tg-AD	20 mg/L in drinking water	Short treatment: 3 months Long treatment:	• Cognitive improvement (long treatment) • Reduced microglial activation, restored TNFα and IRS1/IRS2 expression (short and long treatments)		[51,52]

			5 months			
	5 x FAD	20 mg/kg i.p.	Daily for 2 months	• Improvement of memory impairment • Inhibition of Aβ deposition and neuroinflammation	LANCL-2	[53]

		ABA treatment				
Disease	Animal model	Dose	Duration	Effect	Via	Ref
Parkinson's disease	6-OHDA mouse PD model	10 and 15 µg i.c.v.	1 week (post 6-OHDA injection)	• Improvement of motor symptoms (e.g., muscle rigidity, balance) • Cognitive impairment was not rescued by ABA treatment		[54]
ADHD	Neonatal 6-OHDA lesion mouse model	20 mg/L of drinking water	1 month	• Females: amelioration of pain sensitivity • Decrease of microglia reactivity and normalization of APE1 levels in ACC and pIC • Males: improvement of locomotor hyperactivity		[55]
Anxiety and depression-like symptomatology	Adult male rats	10 µg i.c.v.	1 time	• Improvement of anxiety traits and cognitive performance	PI3K/PKC and ERK signaling pathways	[56,57]
	Subchronic stress mouse model	10 and 15 µg i.c.v.	4 infusions/day for 4 consecutive days	• Improvement of anxiety and depressive-like symptoms • No ameliorative effect on stress-induced learning and memory deficits		[58]
	Acute stress	20mg/kg i.p.	Daily for 6 weeks	• Increment of sucrose intake • Reduction of the mRNA expression of CRH and RAR-α in hypothalamus	RA	[36]
	Chronic unpredictable mild stress	20mg/kg i.p.	Daily for 6 weeks	• Increment of sucrose intake and improvement of FST performance • Reduction of the mRNA expression of CRH and RAR-α in the hypothalamus	RA	
Pain disorders	Adult male rats	5, 10 and 15 µg i.c.v.	1 time	• Increment of the pain threshold (dose-dependent manner)	PPAR-β/δ and opioid signaling pathways	[59]

	Neuropathic rat model (partial sciatic nerve ligation)	20 mg/kg i.p. or 1.5 µg or 15 µg intrathecal	10 days	• Amelioration of pain sensitivity in thermal and mechanical stimulation (systemic and intrathecal administration) • Decrease in microglia and astrocytes reactivity, ERK activity and TNFα levels in the dorsal horn of the spinal cord	LANCL-2	[60]

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Xenomelia: when the body feels foreign

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Received: 26th September 2025 I Peer Reviewed: 1st October 2025 I Accepted: 8th October 2025

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Rare but real, Body Integrity Identity Disorder (BID) is a condition characterized by a strong desire to have a sensory or physical disability, or by feeling discomfort with being fully able-bodied (World Health Organization, 2018, p. 64).

Clinical features of Xenomelia

As "xeno" signifies foreign and "melos" means limb, the term "xenomelia" refers to one of several variations of BID (1). It's a rare pathological condition characterized by an intense and prominent sense of disownership for one or more healthy limbs while acknowledging the absence of any physical defect in appearance or functioning, followed by the compelling desire to amputate the unwanted limb (2). BID encompasses a wide range of functional variants, such as the desire for blindness, deafness, paraplegia, and amputation. Clinicians may mistakenly diagnose a patient with such concerns as psychotic and administer treatment that is not necessarily appropriate for BID due to the lack of acknowledgment or even understanding that such a condition even exists. While prevalence estimates are difficult to determine due to stigma and secrecy, most cases begin before adulthood, and the disorder predominantly affects males (5). Patients typically remain fully aware that their desire is irrational, yet the internal distress is so overwhelming that it dominates daily life and may drive pretending behaviors such as using mobility aids or restricting the limb to simulate disability (3,4).

The classification of BID as a mental disorder was controversial before the release of the International Classification of Diseases (ICD)-11 (5). BID is included under the category "disorders of bodily distress or bodily experience", with the following proposed diagnostic criteria:

• An intense and persistent desire to become physically disabled in a significant way (e.g., major limb amputee, paraplegic, blind), with onset by early adolescence.

• Persistent discomfort or intense feelings of inappropriateness concerning the current non-disabled body configuration.

• The desire to become physically disabled results in harmful consequences.

• The desire to become disabled is not primarily motivated by sexual arousal or by any perceived advantages of becoming disabled.

• The disturbance is not a manifestation of a psychotic process (e.g., desire to amputate a limb because of delusional conviction that the limb belongs to another person), is not due to a primary neurological condition such as post-stroke neglect syndrome, and is not better accounted for by another mental disorder, such as Body Dysmorphic Disorder or Factitious Disorder.

While some theories highlight the role of early exposure to disability, others emphasize possible psychodynamic mechanisms or neurodevelopmental disruptions. Psychodynamic formulations have suggested that BID and Gender Identity Dysphoria (distress that may occur when a person's biological sex and gender identity do not align) are similar (6), resulting from an "erotic target location error" (ETLE) (i.e. a man sexually attracted to a female amputee who experiences an ETLE might want to become an amputee, reflecting the inversion of the erotic target onto the self)(7). However, while most BID sufferers trace their desires to childhood exposure to an amputee, a considerable minority of BID sufferers claim that their desire for amputation and pretending behavior began before any actual exposure to an amputee.

The neurological puzzle of BID

A study by Ramachandran & McGeoch (2007) (8) hypothesized that the cause of BID is a functional issue with the right parietal cortex. They contend that BID results from a decoupling of the actual physical body parts that this region of the right parietal cortex typically represents from the genetically based scaffolding of one's body image. Given that the majority of BID patients date their symptoms to their early childhood, a genetic basis for this uncoupling would make sense. Moreover, tactile stimulation of areas above and below the desired amputation line resulted in statistically reduced activity according to magneto encephalography scans (2) in the right superior parietal lobule, a part of the brain thought to combine various sensory inputs into a coherent body image (4). More recently, an fMRI study by Zapparoli et al., (2025) (9) showed that individuals with BID showed higher neural activations specifically for the stimulation of their left leg in a large cortical and subcortical neural network primarily associated with rewarding and pain stimuli compared to healthy controls, suggesting a pathological relationship between altered neural representations of the body map and the brain reward system in BID.

Treatment challenges and emerging possibilities

A patient who has a strong, ongoing desire to lose their physical ability poses a special clinical difficulty. Given the rarity of BID, it is probable that most clinicians will first rule out other diagnoses in the differential (e.g., psychotic disorder, body dysmorphic disorder, paraphilia, factitious disorder). Diagnostic examinations should also involve a basic screening neurological examination to help rule out primary neurological pathologies and determine potential alterations in the sensation or functionality of the 'target' body part. A diagnosis of BID should also consider the person's motivations for wanting to be disabled, age of onset, potential triggering situations (such as childhood encounters with other disabled people), assessment of reality testing, history of pretending behavior, and other factors. Safety must also be carefully evaluated, considering past self-disability acts or attempts, their effects, as well as present and upcoming plans to fulfill one's wish to be incapacitated.

There are only a few statistics on BID therapy. There are reports of psychotherapy for 36 BID patients (10,11), including one novel cognitive-behavioral intervention designed specifically for this disorder (12), which included cognitive restructuring and behavioral elements to reduce the pretending behaviors of being disabled; however it did not decrease the intensity of the desire for an amputation. Similarly, despite one trial of fluoxetine helping to partially reduce an amputation desire (13), 22 reports of pharmaceutical trials have not shown much promise (12). Since vestibular caloric stimulation, which raises activity in the contralateral parietal cortex, has successfully but transiently treated the post-stroke conditions somatoparaphrenia (denial of limb ownership) and anosognosia (denial of impairment), it has been hypothesized that this technique may temporarily ease BID symptoms (8). The few people who underwent this treatment, however, did not experience any relief, not even momentary respite (14). Recent experimental approaches (e.g., augmented reality-based exposure or neuromodulation) remain in early, exploratory stages without established clinical efficacy (15). Given the lack of empirical data for any treatment, It would be advantageous to develop experimental protocols using carefully chosen BID patients who had failed psychotherapy and medication trials to study the disorder’s genesis, phenomenology, and therapy.

Path forward

A sophisticated treatment strategy and thorough research are necessary for BID/Xenomelia, an uncommon and serious condition. Although formal inclusion in the ICD-11 is a step in the right direction, there are currently few evidence-based treatment options available, and additional research is desperately needed in order to assist those who continue to suffer. Notably, developing novel models of body representation and neuropsychiatric alterations may constitute a first step towards understanding this disorder.

Note: This work is an adaptation of Léa Chibany’s master’s thesis, completed at Sapienza University of Rome under the supervision of Prof. Laura Piccardi and Dr. Alessandro Von Gal.

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Wait, what? The everyday lives of ADHD minds

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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.

It's 9:28 am. You're 11 and you're back in school. Your notebook is open and you're sitting at your desk. The biology teacher is explaining the importance of bees in maintaining ecosystem stability. You really do find bees fascinating, at least, you did a moment ago. Now your eyes drift to the window: "I should remember to call my grandma later, I forgot again last night. The sky is so sunny, maybe I can play football this afternoon". You snap back, wanting to rejoin the world of bees, but the teacher has already moved on. "Crap, I missed it". You try to catch up, but your pen suddenly seems more interesting. Click, unclick, click, unclick. The rhythm calms you for a second, until you hear your classmate whisper. You wiggle in your chair, your legs bouncing. The room feels too quiet. "Wait, who was I supposed to call again?".

But you're not the only one in that room. Out of the 30 kids that are in your classroom, at least one more is fighting the same invisible battle. Struggling to hold their focus, forgetting simple tasks, and drifting into daydreams. That constant war between curiosity and distraction. This is what a person living with Attention-Deficit/Hyperactivity Disorder (ADHD) can feel like.

What is ADHD?

ADHD is more than a moment of distraction in class; it is a neurodevelopmental condition that affects attention, impulsivity, and activity regulation across life. Although it is usually diagnosed in school-age children, ADHD can occur at any age (1). Globally, ADHD affects 5-7.2% of youth and 2.5-6.7% of adults. While the male-to-female ratio is about 4:1 in children, in adulthood it narrows to nearly 1:1 (2,3).

ADHD is thought to be the result of a combination of genetic and environmental factors. Genetic contribution is estimated to range from 60-90% (4,5). Genes regulating neurotransmitter systems, particularly those involving dopamine and serotonin, such as DRD4, DRD5, SLC6A3, SNAP-25, and HTR1B, have been implicated in ADHD (4). Beyond genetics, environmental risk factors such as perinatal complications and exposure to environmental toxins, such as heavy metals or pesticides, during pregnancy may contribute to the disease vulnerability (5).

The DSM-5, known as the standard classification of mental disorders, classifies ADHD into three subtypes. The inattentive type (ADHD-I), characterized by difficulties sustaining attention. The hyperactive/impulsive type (ADHD-H) involves excessive restlessness and impulsive decision-making. The combined type (ADHD-C) includes features of both inattention and hyperactivity/impulsivity, often making it more impairing in daily life. Among these presentations, ADHD-I is the most common, followed by ADHD-H and ADHD-C (3). This variability means that ADHD can look very different from one individual to another, sometimes making recognition and diagnosis challenging.

A common myth is that ADHD can suddenly appear in someone because of lifestyle. However, ADHD is a neurodevelopmental condition, meaning a person is born with it, even if symptoms are not obvious until later. That said, modern habits such as constant digital stimulation, poor sleep, or high stress can certainly make attention and self-regulation worse, both in people with ADHD and those without it. These factors do not “cause” ADHD, but they can mimic or amplify attention difficulties, sometimes making the distinction harder in clinical practice. Recognizing this difference is important because while lifestyle changes can improve concentration for anyone, ADHD itself requires a broader, individualized approach to management.

Not just about children: ADHD in adults

When most people picture ADHD, they imagine a restless child who can’t sit still in class. But ADHD is not only present in children; it follows people into adulthood, and for many, it goes unrecognized. Imagine that the distracted schoolkid we met earlier is also bright, high-performing, getting top grades, and never causing much trouble. Parents and teachers may never suspect. Besides, masking and compensation strategies are not limited to high achievers; people with ADHD across different abilities often hide their struggles. In fact, up to 75% of adults with ADHD remain undiagnosed.

This matters because ADHD in adults manifests differently: while hyperactivity is often more obvious in childhood, inattention and executive functioning difficulties tend to become more prominent during adolescence and adulthood. Adults with ADHD may struggle to sustain attention during meetings, follow through on goals without external pressure, prioritize when everything feels urgent, or manage time effectively. On the surface, these may seem “stress symptoms,” but for many, they are lifelong patterns of unproductivity.

The consequences are serious. A U.S. national survey reported in 2006 that only 11% of adults with ADHD were receiving treatment. Untreated ADHD in adulthood is linked to higher school dropout rates, unemployment, financial difficulties, relationship breakdowns, and even greater risks of substance abuse, accidents, depression, anxiety, and suicide.

Many adults mask their ADHD for years with overachievement, perfectionism, or people-pleasing. They build elaborate systems, micromanage their calendars, and push themselves until burnout. When these coping mechanisms begin to fail, especially in midlife, it’s easy to blame oneself. Yet often, what feels like personal failure may be actually ADHD, a difference in brain wiring that has been there all along, just without a name.

What is happening in an ADHD brain?

It may look like a person is simply "not paying attention." But inside the ADHD brain, things are more complex. Research shows that levels of certain brain neurotransmitters, especially dopamine and norepinephrine, are lower in people with ADHD (4). These neurotransmitters act like messengers: dopamine helps regulate reward, motivation, and focus, while norepinephrine is linked to alertness and sustaining attention. When their balance is disrupted, the brain's ability to filter distractions and stay on task becomes more difficult.

Brain imaging studies suggest that ADHD does not affect one single area of the brain, but rather a network of regions that struggle to coordinate efficiently. These include the frontal cortex, which is responsible for planning, organization, and self-control; the limbic system, which regulates emotions and attention; the basal ganglia, which act as a relay station between brain regions; and the reticular activating system, a key hub for arousal and alertness. When these systems are not working synchronously, it can lead to difficulties with focus, mood regulation, impulsivity, and hyperactivity.

Together, these brain differences help explain why ADHD is closely linked to executive functioning difficulties. While all ADHD subtypes experience some form of executive dysfunction, the intensity and expression vary depending on the individual and factors such as gender, temperament, or co-occurring conditions.

ADHD also impairs auditory processing, meaning a person may miss key details even if they are trying to listen (6). Sensory processing difficulties are also frequent: people may be overly sensitive to touch, light, or sound, or, on the contrary, seem under-responsive (7). For example, a noisy classroom that most kids can ignore might feel overwhelming to a child with ADHD, making concentration nearly impossible. Interestingly, sensory sensitivities also appear linked to higher levels of anxiety, and girls with ADHD tend to report more touch sensitivity than boys (7).

In short, the ADHD brain works under very different rules of attention and regulation. What looks like a child being "distracted" is in fact the distinct neurobiological patterns that shape how a person experiences, interprets, and responds to the world around them.

How is the disease diagnosed?

A proper ADHD assessment involves several steps. Clinicians interview the child and parents, collect teacher reports, and use questionnaires to measure attention, impulsivity, and hyperactivity in different settings. Sometimes, cognitive or neuropsychological tests are added to rule out other conditions. There is no single "ADHD test"; the diagnosis relies on consistent behavior patterns, developmental history, and how much symptoms interfere with daily life

Because the signs of ADHD can be subtle or mistaken for other problems, many people are not diagnosed until later in life. Some children are overlooked if they are quiet or high-performing, while others struggle more clearly as academic and social demands increase in adolescence.

In adults, hyperactivity often decreases, but problems with focus, organization, and impulsivity remain. Diagnosis can be challenging because ADHD symptoms may resemble anxiety or mood disorders, and many adults experience both. Women, in particular, are frequently overlooked, since they often present inattentive symptoms such as daydreaming, forgetfulness, or mental fatigue. Because these behaviors are not always recognized as signs of ADHD, they are often mistaken for stress or personality traits. Many adults only realize they have ADHD when they face work responsibilities, relationships, or even parenting challenges. In these cases, diagnosis often comes as both a shock and a relief, explaining a lifetime of difficulties that were previously blamed on personality or effort.

Can we treat ADHD?

ADHD does not simply disappear with age, but it can be managed effectively. Treatment usually combines behavioral strategies, educational support, psychotherapy, and, in many cases, medication. In children, family and teachers' involvement are crucial, while in adults, coaching, quiet workspaces, and task management tools may also be beneficial.

Medication, particularly stimulants, can be very effective in improving focus, self-control, and emotional regulation. The most common treatments include methylphenidate (known as Ritalin or Concerta) and amphetamines, with atomoxetine as a non-stimulant alternative. These medications act on the brain's dopamine and norepinephrine systems, helping strengthen the circuits involved in attention and executive functioning (8,2). Importantly, these drugs are prescribed to manage ADHD symptoms, not to enhance performance in people without the condition. Misuse for "boosting productivity" is a separate issue and should not be confused with medical treatment.

While stimulant medications are often safe and effective, treatment decisions must be individualized. Some experts have raised concerns about overdiagnosis and overprescription, but evidence shows that intentional misuse accounts for only a small fraction of cases. In fact, focusing too heavily on "overdiagnosis" risks creating barriers to care and reinforcing stigma, discouraging people from seeking help when they need it.

Medication should always be part of a broader approach that can include behavioral therapy, psychoeducation, skills training, and family or workplace support. For many, the most effective strategy is a combination of medication and psychosocial interventions, addressing not only attention and impulsivity but also organizational challenges, emotional regulation, and co-occurring conditions.

What to take with you

That kid staring out the classroom window may not process information the same way you do, but that doesn't make them lazy or less intelligent. ADHD is not about willpower; it's a different way of living the world. If left unrecognized, ADHD can affect every part of life: school, work, relationships, and mental health. What begins as missed homework can grow into years of struggle and self-blame without help.

But it doesn't have to be this way. Standard treatments such as therapy, skills training, and sometimes medication can make daily life much easier. For a child, that might mean keeping up in class. For an adult, it might mean better focus, organization, and healthier relationships.

Raising ADHD awareness means fewer children left behind, fewer adults suffering in silence, and more people empowered to live their lives to their full potential.

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Women's Voices: inspiring the neuroscientist community

Christelle Glangetas

Sara Carracedo[1]
[1] Postdoctoral researcher at the IMN, Bordeaux Neurocampus

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 interviewed **Christelle Glangetas**, a senior postdoctoral scientist at the IMN. Originally from Guadeloupe, Christelle moved to France to complete a Master's in Neuroscience at the University of Bordeaux, followed by a PhD at the Interdisciplinary Institute for Neurosciences (IINS), where she studied the role of neuronal plasticity in anxiety regulation. During her first postdoctoral position, she worked in Switzerland, focusing on motor and anxiety circuits in pathological conditions. She is now a senior researcher at the IMN, where she leads a research axis on the neuronal mechanisms underlying anxiety. In recognition of her scientific work and outreach efforts, Christelle received the Marian Diamond Prize from NeuroPIC this year. In this interview, she shares her academic journey and reflects on some challenges of securing permanent positions in academia.

Sara Carracedo: Could you please introduce yourself and your academic path?

Christelle Glangetas: I am a senior postdoctoral scientist working at the IMN in Bordeaux. My primary research interest is to understand how the brain shapes emotions and, inversely, how emotions shape brain plasticity. I obtained a PhD in Neurosciences at the University of Bordeaux in 2014, at the Interdisciplinary Institute for Neurosciences, where I investigated the role of neuronal plasticity in anxiety control.

Then, I moved to Switzerland to the team of Camilla Bellone as a postdoctoral researcher, where I worked on motor and anxiety circuits in physiopathological conditions (Huntington's disease, Autism Spectrum Disorders).

In 2018, I joined the Institute of Neurodegenerative Diseases (IMN) with a postdoctoral fellowship from the Fondation de la Recherche Médicale (FRM). I work in the team led by Jérôme Baufreton and François Georges. During the last six years, I have built a research axis on the neuronal mechanisms underlying anxiety and anxiety-related disorders that I hope to pursue in this team as an assistant professor.

Sara Carracedo: What is your current research focus at the IMN?

Christelle Glangetas: I am developing several scientific projects, and their common point is to understand how neuronal circuits control social and emotional processing. In particular, I am studying the role of different neuronal populations of the insular cortex (insula) in social and anxiety behaviors.

Sara Carracedo: You received the 2025 Marian Diamond Prize from the NeuroPIC. How do you think prizes like this contribute to supporting and promoting women in neuroscience?

Christelle Glangetas: First, I have to say that I was really happy to receive a prize from the Bordeaux Neurocampus community, which recognizes my scientific work and my contribution to scientific outreach. This prize allowed me to share my latest research on the insula and social preference as an invited speaker at the Bordeaux Neurocampus Day. It was a valuable opportunity to network with colleagues and demonstrate my expertise. Being a laureate of the Marian Diamond Prize also increases my visibility more widely, which is an essential step in supporting and promoting women in neuroscience.

Sara Carracedo: As a senior postdoc, have you faced any specific challenges or structural barriers to securing a permanent research position in academia?

Christelle Glangetas: Yes, I faced barriers to securing a permanent research position in academia, and I am still struggling as a senior female postdoc scientist.

It was a question that I asked myself: Why do I not have a permanent position given my motivation, my commitment, and my success? Why?

We all know that neuroscience is a very competitive field, and it is even harder for female scientists. In France, only a limited number of research positions are available each year, and assistant professor positions can be even rarer. We have few positions and many candidates! Science needs more financial support from our government agency; that is obvious.

But still, why? I have an excellent profile. With all humility, I am an excellent researcher, and I really think that teaching is made for me. I would be a great assistant professor at the University of Bordeaux. I am convinced that my fifteen years of expertise would benefit the students and the scientific community.

I still do not fully understand why I face so many barriers in French academia, and I have stopped asking myself this question. I continue to enjoy science with my colleagues, students, and train myself to learn new skills and build other opportunities. So, it is the last chance for the research academia to keep me!

Sara Carracedo: What advice would you give to women aiming for long-term academic careers in neuroscience?

Christelle Glangetas: Prepare for your success. It is good to plan your next scientific experiment, the one for tomorrow, the one you want to do next week, but see further, see bigger. Take advantage of this rich professional environment (Bordeaux Neurocampus and the University of Bordeaux). Think about your career plan. Create your opportunities. Finally, be yourself, do what you like and what you are good at.

NeuroPath: exploring careers beyond academia

Pablo Duarte Flórez, Medical Science Liaison

Sara Carracedo[1]

[1] Postdoctoral researcher at the IMN, Bordeaux Neurocampus

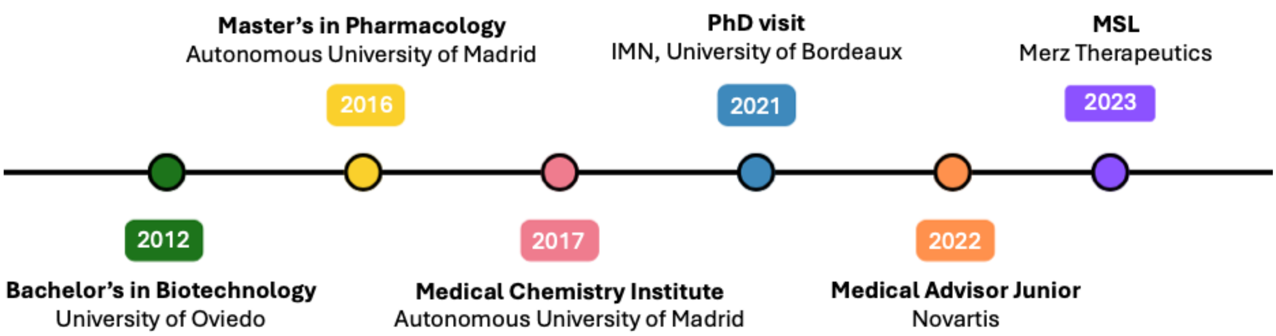
The world of science offers many exciting paths, and academia is just one of them. Each year, both the public and private sectors actively seek PhD graduates to fill diverse roles. However, many of them may seem unfamiliar to most of us. At Brainstorm, we want to help you explore career options that align with your interests, and aspirations.

That's why we created NeuroPath: a section dedicated to highlight scientific related careers outside academia. We reached out to professionals, who like us, have earned a PhD in neurosciences, most of them from the Neurocampus, but chose to apply their expertise in different fields. Through their stories, they share insights into their career journeys and practical information regarding their current positions.

Science is a lifelong pursuit, but the path you take is yours to choose.

Follow the one that excited you the most!

This month in *Neuropath*, we spotlight **Pablo Duarte Flórez**, working as a Medical Science Liaison (MSL) at Merz Therapeutics. Originally from Spain, Pablo did a PhD in Pharmacology during which he conducted an internship at the IMN at the University of Bordeaux. Nowadays, Pablo works in the interface between science and clinicians, where he bridges scientific knowledge with clinical application. Passionate about medical education and communication, Pablo plays a key role in supporting scientific strategy and engaging with healthcare professionals in the field of neurology.



Are you interested in knowing more about the MSL job as a career path? Then this section is for you!

Medical Science Liaison

Pablo Duarte Flórez

I serve as the scientific face of the company, acting as a bridge between pharmaceutical companies and the medical community

What is your role outside about?

As MSL, I connect with healthcare professionals to share scientific information and I am involved in the company's medical strategy. I also represent the company in hospitals, congresses, and medical institutions.

Why did you choose this professional path?

I chose this career path because it allows me to stay closely connected to science. It blends my scientific background with interaction in the clinical field, offering a dynamic environment. Unlike academic research, this role has a more applied clinical focus, which makes the impact of my work feel more immediate and tangible.

What's a matching profile?

Someone sociable and a strong communicator. You must have a strong scientific understanding and organizational skills. You should feel comfortable in dynamic as well an adaptable and curious person.

Main Responsibilities

- Visiting hospitals and health centers
- Discussing scientific information with doctors and pharmacists
- Providing internal and external training
- Participating in medical congresses and events
- Support clinical research
- Provide medical insights
- Social interaction and communication of scientific topics

Requirements

A PhD is highly recommended (though not mandatory)

Bachelor's degree in a relevant scientific field

Career Progression

Strong potential in the pharmaceutical industry

MSL -> Medical Advisor -> MSL Lead -> Medical Manager

Working conditions

Work environment: Excellent, employee well-being is prioritized

Pressure level: Varies with workload, high pressure and responsibility

Work-life balance: Balanced, but willing to travel

Salary: Good, starting around €40,000-45,000/year

Do you have further questions?

Contact Pablo at pabloduarte24@gmail.com

Do you have some advice for PhDs interested in this path?

If you're considering an MSL role, talk to people already in the position to understand the reality of the job. Explore job descriptions and keep an open mind; rather than large, well-known companies, small and mid-sized companies can be great entry points, offering more hands-on experience and room for growth. Networking can also help you stand out.

Out of sight tenants
Interview with John Cryan

Juan Garcia-Ruiz[1]
[1]PhD student at Neurocentre Magendie, University of Bordeaux

Over four and a half billion years ago, the first life forms began to emerge from hydrothermal vents at the bottom of the oceans: prokaryotic microorganisms, the ancestors of bacteria. This occurred only two hundred and sixty thousand years after the origin of the Earth. In contrast, the first homo sapiens did not emerge until much later, about three hundred thousand years ago. In relative terms, if we imagine that one hour has elapsed since the formation of the Earth until today, the first prokaryotes appeared 0.2 seconds after the formation of the Earth while the first homo sapiens appeared 59 minutes and 59 seconds later. Our passage on Earth is insignificant from a temporal point of view if we compare it with that of bacteria, which have lived almost the entire history of the Earth. Bacteria are no longer those insignificant microorganisms that we only think of when we have an infection. But it doesn't end there. Bacteria have not only lived much longer than humans, but they are also part of us (or we are part of them). Let's face reality: there are more bacterial than human cells in our body. In a way we are like mythological beings, except that unlike the centaur or the faun, we often forget our other half (and we do exist).

To better understand our relationship with our prokaryotic tenants, we talked to John Cryan, Professor at the University of Cork in southern Ireland, where he is also Vice President for Research and Innovation. John was trained in neuropharmacology and focuses his research on stress-related disorders and the brain-gut microbiota axis.

Juan García Ruiz: What exactly is your current research about?

We are working on trying to understand the relationship between the microbiome, which is the strains of bacteria we have in our gut, and the brain and behavior. We want to answer to two big questions. One is understanding how microbes can communicate with the brain, and applying state of the art neuroscience tools to try to disentangle these routes of communication. Secondly, we try to translate our findings in animal models to the human condition so we can understand what works best to our gut.

JGR: How relevant is your research for society?

JC: This is really important because if we place this research in an evolutionary context, the microbes were there first. There never has been a time where the brain existed without microbial signals. Understanding how this coevolution has occurred and to what level have signals from the microbiome been able to shape our brain circuits is essential for understanding every aspect of our lives, because if our microbes are shaping our brains, they are controlling all of our decisions and therefore they impact everything that we do.

JGR: What's the estimate number of microbes we have in our guts?

JC: We have more microbes than human cells, the ratio is about 1,3 to 1. That would also include virus, archaea and whatever else. In terms of genes though, we are more than 99% microbials. That's very humbling, it's 20 years of the human genome project and we are only dealing with 1% of all the genes.

JGR: How do you study the microbiota-gut-brain interaction in the lab?

JC: We have to be a bit reductionist so we can look at every part individually. We study the microbiome itself by looking at its genomes, its metabolites, its functional capacity. Then we look at the next layer for the microbes, and we study the gut epithelium to try to understand how it's interacting with the immune system within the gut, the enteric nervous system, the vagus nerve, the hormones and so on, and see how all of this can have confluence to the brain. We study most things in the brain with traditional tools, in models and in humans, and we eventually integrate human brain imaging techniques.

JGR: What do we know about the interaction between the microbiota and the brain so far?

JC: We know very little overall. We are really at the beginning of it. From my research I know that the microbiome in early life is very important for sculpting brain development. So in our models we take away the microbiome and we interfere with brain development processes, that's really clear. We know the microbiome is involved in functions such as prefrontal cortical myelination patterns, adult hippocampal neurogenesis, the integrity of the blood brain barrier, and the functioning of microglia, which are the brain immune cells. What we don't know is how. But it doesn't stop at early life. We also think that the microbiome is contributing in some ways to some of the neuroinflammatory effects that occur with aging. Knowing this, we can either target the microbiome to improve developmental processes or to slow down aging.

JGR: How variable is the microbiota in human?

JC: The way I see microbiome is almost like a signature of what happened to you in the last proximal and not so proximal time. It's variable. It's very influenced by the environment we are living in and the diet. If you eat a lot of very nice Portuguese pastries, you will have a different microbiome than if you drink a lot of Irish Guinness. There's nothing you can do with your genome, except blaming your parents and your grand-parents. Unlike the genome, you can potentially change your microbiome. That gives the patients great agency of their own health, in terms of taking control.

JGR: Our interest for the brain-gut microbiota and publications about this topic have skyrocketed in the last years. It is possible to find all kind of relationships between microbiota and psychiatric disorders in the literature. As an expert in the field, are you skeptical about some of the findings?

JC: I think it's good to be skeptical on this field. There's a lot of healthy skepticism. Extraordinary claims needs extraordinary evidence. Have we got the extraordinary evidence? Probably not yet, but we got really intriguing evidence that is starting to build. In the autism field in particular we see it quite remarkably, but we cannot forget that autism is a genetic disorder, so the microbes are not the whole answer, but they are maybe playing a role in shaping it. Some of the data that has been shown in that regard is quite interesting. I think it's early days. We have to always look at the evidence. The microbiome field is trying to go from correlation to causation. How do we get a causation? We need to do a lot of more basic research, a lot of human research, and a lot of longitudinal research to get there.

JGR: What is the most astonishing discovery you have done or experienced during your professional career?

JC: For me a eureka moment was when we found that mice that grew up without microbes showed a very high hypermyelination in the prefrontal cortex. These mice can actually live longer. I described it a little bit like those studies that looked at how nuns living in convents, in enclose orders, can live into their hundreds. It's kind of the same. If you are not exposed to anything, you have no stress of children, no stress of anything and all you do is pray all day, then you are more likely to live longer, but this is not as much fun! So anyway, discovering that there was hypermyelination in mice without microbes is a remarkable finding because it opens up so many questions. Could we target myelination process in the brain by targeting the microbiome? Or could we somehow understand what is going on in relation to myelination, conductivity of neuronal signals and behavioral changes we find in these mice, which are social deficits? Hypermyelination is also occurring in some autism cases. Not very often, but it's still interesting. That's pretty cool, you can look down to the microscope and see this, that's impressive!

JGR: What led you to do research?

JC: I guess I have always been curious. I probably didn't do real research until I went to university. I studied general science and got very interested in biochemistry. I just got softly into it. I like to see things change, so I like studying behavior. Besides I wasn't a very good biochemist. I remember I was amazed when a friend of mine who was doing studies with drugs at the time showed me what a mouse looked like on extasy. I started to do research on the serotonergic system and behavior. So everything I do is contextualized by how is this affecting behavior. Even though that I cannot see the microbes, I can really see the output and I am very fascinated by that.

JGR: You have hundreds of publications and a very high h-Index. Especially for young researchers, getting started to publish can be tricky. Do you have a piece of advice?

JC: The hardest thing for a young researcher is focusing on the output. You should think about writing a paper as a five figure plan and have this in your head at the beginning. The data can take you in different places and you should always be agile and aware of that. If you focus on how to get there, then you will not be long building paper after paper. I think publications are a sign that you are being productive and that you are output-oriented. Whether you want to stay in academic research, or move into industry, or project management, having a paper shows that you can deliver an angle and wrap something up. One of the biggest problems we have that I try also to tell young people is that sometimes you just have to let it go. Meaning two things: there is an aspiration to try and solve everything, and sometimes you just need to get the finding out there. For instance take myelin paper: we could have spent years and years figuring out the mechanism. It's been five years and I still don't know what's happening. We could have delayed the publication till then, but I thought it was too important to wait. But the other thing I mean by let it go is that sometimes things just don't work, so don't hold on to these things, be flexible, be imaginative. I never worked on microbes really until I came back to Ireland. My colleagues here were doing it for different reasons and I started getting in collaborating with people here. I could have been very snobby and say: "well no I won't work on that, I am working on stress, the brain" and so on. I think instead we should be open, that's how wonderful things can be crafted.

JGR: What's the best advice you got from someone?

JC: I worked in the industry so I spent four years working in Basel, and they were very wonderful years. But my PhD supervisor had said to me once: never work for industry. I was a bit perplexed because he had worked in industry. Then he rephrased it and he said: "work for yourself while you are in industry and as long as you are meeting the industry goals and you keep that you are a scientist, and that you are creative and curious, it doesn't matter who's paying your salary".

JGR: You have participated in the writing of the bestselling *The Psychobiotic Revolution*. Can you talk us about this project?

JC: We wrote this book and for us is now like the new New Testament, it's like our Bible to the world to tell them that we should be thinking more holistic about the microbiome. We tried to get people excited about science. It was published by National Geographic, so it was a very exciting adventure. We wrote it in a way that everyone could read it no matter the background. Also in different languages. We recently published it in Polish, in Chinese and in Spanish: *La revolución psicobiótica* (N. of A: pronounced with perfect Spanish accent). Not French, for the moment.

JGR: In addition of the co-writing of *The Psychobiotic Revolution*, you have edited three books, you are a professor, you are on the editorial board of more than 15 journals, you have received numerous awards for your research and you still have time to do Ted talks. Are you a human being?

JC: Yes, and don't forget that I also have kids! People ask me this sometimes. I am very passionate about what I do, I really love what I do. That makes it all easier. Secondly, I am not really a perfectionist, so I am able to let things go. I feel passion about communication in science, we need to be able to get messages out there, to inform policy and to inform the public about what's going on. Therefore I can get funding. Then I have an amazing team of people who work with me, many Spanish, from Madrid, Barcelona, and Mallorca. So you know we have a very Spanish-Catalan view of the world here. That's quite exciting. I guess I am output-oriented and I try to train people to be outoput-oriented, so we can achieve a lot! We try for excellence and push ourselves. But there's a lot of fun, you enjoy, you make discoveries. Every paper I publish I still get excited about it!

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

JC: My message is going to be for researchers. Research is about understanding that what they will be working on in ten years has probably not even been discovered now. Be open to these discoveries coming down the line. Secondly, break down the barriers we create in research and medicine. Because we talk different languages when we talk about the brain, the gut, or immunology and microbiology. Let's break down these compartmentalisations. Finally make sure that the research has some impact from a whole planetary perspective. Embed research within the systemic development goals of the United Nations. It's really important to use what we do to help create the innovation situations that makes us moving forward.

For more interviews, visit www.neuronhub.org

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Neurofailure

Mito-avengers

This cinematographic neuro failure is the result of a staining of mitochondria in a brain slice from a L1-syndrome mouse. The staining was performed using the dye Mitotracker, and the picture was acquired with a spinning disc microscope.

Ludovica Congiu, postdoctoral researcher

Formations

PhD seminar series

Remember to register to the PhD seminar series. You have until the end of October to register for the first part on ADUM. Every first Friday of the month, you can attend the PhD seminar – a presentation by a guest chosen by the PhD community at the Neurocampus.

To keep up to date with the program, take a look at the Neurocampus website.

Initiation à la clinique

Pour les francophones uniquement.

Le Graduate Program vous invite à aller dans les cliniques en partenariat avec le Centre Hospitalier Charles Perrens et le CHU Pellegrin.

L'initiation à la clinique et aux soins en psychiatrie débutera par une journée théorique le **7 Novembre 2025**, puis 8 demi-journées dans les services de Charles Perrens.

L'observation dans le service des maladies neurodégénératives du CHU Pellegrin débutera par une journée théorique le **17 Novembre 2025**, puis 4 demi-journées dans le service.

2025 COVER CONTEST

WINNER

Yasmin Guerra

Ludovica Congiu

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Editorial board

Aude Verboven

Aude, directly coming from Bordeaux, is a PhD student at the IMN. She previously graduated from the MultiPublic track of Bordeaux Neurosciences Master. She is currently studying the dopaminergic afferences to pain modulating nuclei in the context of Parkinson's disease.

Juan Garcia-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).

Toshiko Sekijima

Toshiko, originally from New Zealand, is pursuing a PhD at Nutrineuro focusing on how the gut-microbiota influences brain inflammation and psychiatric illness. 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 which you can find @toshi.co on Instagram.

Sara Carracedo

Born in Spain, Sara is a Postdoctoral researcher at the IMN. She holds a Veterinary Medicine Bachelor's degree from the University of Santiago de Compostela, the NeuroBIM Master's degree, and a PhD in neurosciences from the University of Bordeaux. Her Postdoc at the IMN focused on understanding the neuroimmune role of P2X4 receptor in Amyotrophic lateral sclerosis.

Daniele Stajano

Daniele Stajano was born in Naples (Italy). He has a Bachelor's degree in Biology and a Master's degree in Neurobiology. After his Ph.D. in neurosciences at the ZMNH of Hamburg (Germany), he joined as postdoctoral researcher the IINS. He is currently interested in molecular mechanisms orchestrating brain maturation in neurodevelopmental disorders such as the autistic spectrum disorder.

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. She is a Postdoctoral researcher at INCIA.

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.

BRAINSTORM

A Journal for the students, by the students

Are you a MSc, PhD or a PostDoc student in neuroscience?

Then you are more than welcome to participate in our journal.

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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.

Don't start to worry, you won't be alone! You will work hand-by-hand with our editors, and we will send you guidelines and a template to make your life easier. Perhaps you would like to know that the best review will get a special prize by June 2025.

If writing is not your thing and you prefer to express yourself through art, we have a place for you too! For each issue we recruit an artist to design the cover page illustration. Remember that microscopic images are also a form of art.

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