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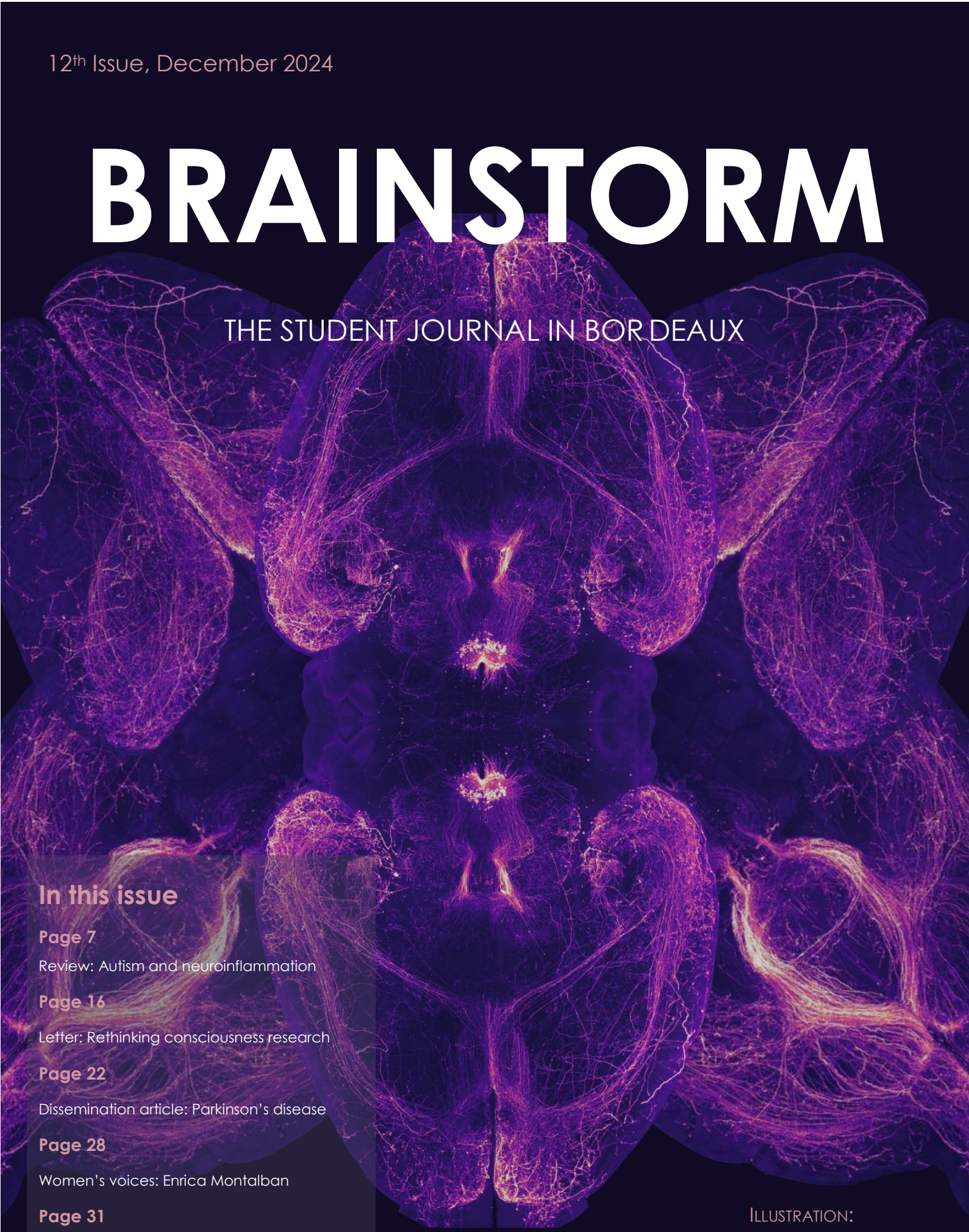

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All authors take responsibility for the content of their publication.

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An unceasing loop: autism and neuroinflammation

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Meera comes from Mumbai (India) and holds a bachelor's degree in Biotechnology from Mumbai and a Master's in Research in Integrative Neurosciences from the University of Edinburgh (Scotland). She is currently a PhD student at the IINS working on how environmental factors, like inflammation, play a role in the progression of neurodevelopmental disorders such as Autism. Beyond her research work, she is actively involved in science communication and outreach programs for kids to cultivate curiosity for science in young minds.

Abstract

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder impairing social interactions, exhibiting repetitive behavior and occasionally showing cognitive impairments. It exhibits a high degree of phenotype heterogeneity, with individuals presenting varied backgrounds, different symptoms, genetic aberrations, and comorbidities. Multiple studies have identified genetic mutations that affect key synaptic or transcriptional elements and hamper neurodevelopment. An active role of immune dysregulation such as hyper-activation of microglia and inflammation in brain regions have also been reported in animal models and human studies. The interplay between synaptic plasticity and inflammation and how one could be a causative or a consequence of another prompted this review.

Keywords

Autism Spectrum Disorder (ASD)/ Neurodevelopmental disorder (NDD), Inflammation, Genetic mutations, Immune activation

Abbreviations

ASD- Autism Spectrum Disorder
BBB- Blood Brain Barrier
CSF- Cerebrospinal Fluid
CNS- Central Nervous System
GI- Gastrointestinal
LPS- Lipopolysaccharide
MIA- Maternal Immune Activation
NDDs- Neurodevelopmental disorders

Introduction

Autism Spectrum Disorder (ASD) is a highly heterogeneous group of neurodevelopmental disorders that exhibit symptoms immediately after birth, and are primarily characterized by impairments in social interactions, stereotypical repetitive behaviors, and intellectual impairments (American Psychiatric Association, 2013). The precise etiology of ASD and its progression remains a challenge for researchers, medical professionals, and caregivers. Initially, a gene-centric approach was employed to uncover the underlying causes of ASD [1]; however, the heterogeneity observed in its phenotype indicated the involvement of additional factors. Recent studies suggest that ASD could be a result of systemic abnormalities and not only brain-specific impairment [2, 3], which will be further discussed in the article.

Gene studies have found that impairments in chromatin remodeling [4], DNA mutations [5], and mRNA transcription and translation [6] are the underlying causes of ASD. Many of these genetic aberrations affect the proteins associated with morphological, cellular, and synaptic functions in neurons.

Neurodevelopment is a complex process that involves the development of essential and coherent brain circuits, clearing out excess synapses, and strengthening important circuits. Impairment of synapse-associated genes that code for receptors, adhesion molecules, and scaffolding proteins can hamper neurodevelopment, which may in turn cause neurodevelopmental disorders (NDDs) [7]. Synapses are abundant at birth and are cleared during development by an activity-dependent mechanism called synaptic pruning. Impairments in synaptic pruning have been demonstrated in ASD models with abnormal synaptic density [8].

While gene mutations and alterations remain the best-explored causes of ASD, newer studies have discovered links between other factors severity of ASD phenotypes.

that were initially thought of as comorbidities. Inflammation has been found to be one such candidate, and neuroinflammation at critical stages of development has been shown to hinder normal brain development. Various post-mortem studies and studies from human CSF and brain tissues have shown higher activation of microglia and higher levels of markers of neuroinflammation [9]. Furthermore, evidence of prenatal maternal infections [10], early postnatal infections, and disturbances in the gut-brain axis [11], which have a strong positive correlation with the ASD phenotype, indicates its causal role in the progression or development of this phenotype.

ASD is also associated with comorbidities, such as gastrointestinal troubles (GI) [12] and systemic inflammation, demonstrating that ASD and GI troubles could share underlying biological processes [13]. These biological processes may include immune dysfunction [14], abnormal intestinal permeability [15], and microbiota abnormalities [16]. Increasing evidence of autoantibodies in ASD patients [17], evidence of maternal infection negatively affecting ASD development [18], maternal autoantibodies infiltrating the placenta and BBB [19], and stress causing preterm birth has been shown to increase the odds of ASD development in children [20].

Many theories have focused on the pathogenesis of ASD, and subsequent questions have emerged in response to evidence showing the interplay between inflammation and ASD. This review aims to broaden the horizon of ASD etiology and not only focus on genetic aberrations as a causative factor but also as a factor in inflammation, with the help of the more recent advancements pointing to its involvement in the etiology, progression, and severity of ASD phenotypes.

Methods

A preliminary search for relevant articles was done using reviews found on PubMed with combinations of the following terms: "(Autism OR ASD) AND (Inflammation OR Microglial activation OR Epigenetics) AND/OR (Genetic Mutations)" (filtered to last 10 years).

The sorting and selection of articles were then performed using the following terms ((Autism OR ASD) AND (Maternal inflammation OR preterm birth OR gut-brain axis dysregulation)) of MeSH terms, now selecting research articles and bioRxiv papers. The articles and their relationship with one another were visualized using ResearchRabbit, where some more relevant papers were added using the same key terms. There were no strict limitations on the year of publication of research articles.

Results and discussion

ASD and genetic risk factors

While numerous reports have indicated the involvement of external factors in ASD etiology, genetics should not be discounted.

In the early 2000s, multiple loci on different regions, including 7p, 16p, and 2p chromosomes, were identified to be implicated in ASD (International Molecular Genetic Study of Autism Consortium, IMGSAC). However, focusing only on these regions has not yielded conclusive results, and the development of high-throughput sequencing in the last decade and the formation of large cohorts starting in 2010 changed the horizon. The multigenic etiology of ASD provides clearer results. While these studies identified multiple genes from the brain implicated in ASD, they can broadly be divided into two categories: those that function in synapse formation, transmission, and plasticity, and another group of genes involved in transcriptional regulation and chromatin remodeling [4].

Synapse formation, synaptic transmission, and plasticity

Many genes that play a role in maintaining healthy synapses, such as neurexins, neuroligins [21], cadherins [22], and presynaptic vesicle protein genes, such as synapsin 1 and 2 [23], are implicated in ASD. In addition, other genes are regulated in ASD, such as scaffolding proteins such as Shank3 [24], Ras-GTPase activating protein SYNGAP1, receptors such as GABRG3, and members of potassium voltage-gated channel families (2KCND2, KCNQ3, and KCNQ5) [23].

Transcription regulation and chromatin remodeling

MECP2 is a chromatin modifier that regulates many genes that are crucial for synaptic functioning, including brain-derived neurotrophic factor, insulin-like growth factor binding protein 3, cyclin-dependent kinase like 1, and GABR3. It also modulates glutamatergic synapse formation [25], and phosphorylation of its promoter leads to lower levels of MECP2 in the prefrontal cortex in ASD patients. [26, 27, 28] E3 ubiquitin protein ligase targets proteins for degradation, and it is involved in Wnt signaling, which is crucial in axis patterning in neurons and embryonic development [29]. The most well-known causal gene of ASD affecting transcriptional pathways is the Fragile X Messenger Ribonucleoprotein [30]; mutations in this gene cause abnormal RNA-editing enzyme activity.

The above-mentioned mutations include both rare variants and de novo mutations as well as common variants that may underlie ASD pathophysiology.

ASD and inflammation

In recent years, a strong association between ASD and inflammation has been established, and new studies continue to support this. There are multiple reports in the literature of ASD patients that have a hyper-inflammatory profile with an increase in TNF-α almost 50-fold in the CSF [31], IL-6 in the brain [32], and IL-1beta and IL-8 in the plasma [2]. Vargas et al. found an elevation in the levels of pro-inflammatory cytokines in the brain tissue as well as in the CSF of living ASD patients [9].

Post-mortem studies are consistent with these findings, showing the over-activation of microglia [9]. Microglia are resident macrophages found in the central nervous system (CNS) that react to external cues by changing their activation state.

Thus, activation of microglia is a simple yet effective marker of infection or the non-homeostatic condition of the brain. In addition, molecular studies have shown a reduction in certain synaptic proteins, such as PSD95 and SYN1 [33], while immunohistochemistry studies in the prefrontal cortex showed active microglia in 5/13 ASD cases [34,35]. Microglia are known to mediate synaptic pruning and their aberrant activation leads to abnormal synaptic development [36, 37].

Apart from the direct effects on the nervous system, there are other indirect mechanisms that may cause inflammation.

Maternal infections

Maternal immune activation (MIA) has been established to have a role in immune activation of prenatal children inducing behavioral dysregulation [38] and inflammatory states [39]. These findings are supported by numerous animal studies [40]. Bauman et al. showed that poly:IC injections in pregnant rhesus monkeys led to repetitive behavior and atypical social interactions in offspring, which are known features of the ASD phenotype. Lipopolysaccharide (LPS) is found in the outer membrane of gram-negative bacteria and can induce inflammation. Inducing Inflammation by injecting LPS into pregnant mice led to a reduction in the receptors needed for complement-mediated synaptic pruning, where the complement cascade, a part of innate immunity, causes microglial activation and marks the synapses (in this case) for phagocytosis [41, 42]. Maternal obesity and asthma have also been found to play causative roles in ASD. [43]

However, MIA is not always necessary for ASD development in the offspring. Some reports have indicated that elevated pro-inflammatory cytokines (IL-6 and IL-17) in pregnant mice are sufficient to give rise to autistic traits [44, 45]. Similar observations were also found in humans by Jones et al. in 2017 [46], where mid-gestational elevations in cytokine levels were found in mothers of children with ASD.

Post-natal injuries

Preterm birth can result from placental dysfunction or intrauterine infections, which could result in hyperinflammation and anoxia in the offspring, possibly leading to ASD [47, 48].

Oxidative stress

Recent studies have focused on the relationship between oxidative stress (OS) and ASD. Reports have shown an increase in OS markers, lipid peroxidation markers, and mutations that affect antioxidant pathways causing OS [49].

Discussion

Our understanding of the mechanisms underlying ASD has greatly improved over the last decade. However, an important limiting factor was the lack of a sufficiently large sample size in these studies. In addition, the complexity of disorder makes it difficult to draw conclusions and develop models that accurately depict the disorder condition. Various studies have also shed light on the sex-specific severity of ASD and sex-specific effects of maternal infections. Human ASD studies consider variables such as age, onset of maternal infections, sex, and weight of the baby and mother at birth. Thus, achieving larger sample sizes after sorting requires collaborative efforts. More focus on animal models that manipulate specific pieces of the ASD puzzle will help decipher individual causatives; however, decades of work in this area can be easily foreseen.

Moreover, reports in ASD show brain volume changes, as well as modifications in synaptic densities and dendritic spine morphology, which lead to an impairment of synaptic transmission. The role of microglia as mediators of synaptic pruning and its hyperactivation in ASD conditions suggests a very strong link between hyperinflammation during critical periods of neurodevelopment and improper synaptic pruning.

More recent evidence suggests the involvement of stress or postnatal allergen exposure in ASD-like

behavioral phenotypes [54, 55]. This leaves several open questions: (a) Which factor comes first, inflammation or the ASD phenotype? (b) Can these two factors be independent of each other? (c) If they coexist most of the time, does one factor worsen the other, making it an unceasing loop and another challenge in finding effective therapeutics?

Conclusions

This review aimed to portray inflammation not just as a comorbidity of ASD, but also as a factor that plays a critical role in its pathogenesis, severity, and progression. The above-mentioned studies have shown strong and significant links between ASD and inflammation. The underlying mechanisms remain undiscovered; however, the focus on GSK3-beta [50], which plays a role in synaptic plasticity and neuroinflammation, has increased in recent years. Upregulation of GSK3-beta was found in Fragile X syndrome [51], and ablation of GSK3-beta in brain regions caused a reduction in dendritic spine density [52], which is in line with the abnormal synaptic pruning reported in ASD.

ASD is a neurodevelopmental disorder; therefore, time-sensitive and longitudinal studies are needed to identify the mechanisms underlying this heterogeneous phenotype. Pilot studies where intervention with intravenous immunoglobulins improved behavioral and cognitive endpoints in 14 ASD patients and reduced pro-inflammatory marker activations [53] demonstrated that immunotherapy could be the next therapeutic candidate to reduce the negative phenotypes and improve the lifestyle of ASD patients. It is also crucial to identify the degree of damage to neurodevelopment by inflammation and genetic mutations to further inform timely therapeutic interventions to ameliorate severity.

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Rethinking consciousness research

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Humanity's desire to understand the nature of consciousness is old as civilization itself. Neuroscience is a direct consequence of this pursuit of the self and has provided valuable insights into what makes us human and different from other animals. Many will say that the one thing that tears us apart from the rest is our consciousness, making it an unique phenomenon. Yet it wasn't until the late 1990s that the study of consciousness began to gain legitimacy and importance (1). As a result, consciousness is still perceived and studied as any other high-order process, despite the fact that its existence challenges the foundation of science itself. The goal of this letter is to offer a perspective on how the scientific community is currently addressing consciousness and challenge research to approach the subject differently.

Consciousness science is currently practiced as an interesting mix of philosophy, mathematics, computational sciences and neuroscience. The neuroscientific approach to consciousness seeks to explain how the brain's structure and activity give rise to subjective experiences. Growing empirical and theoretical work is steadily advancing our understanding of the complex neural circuits involved, bringing us closer to resolving the soft problems of consciousness: how we become aware of sensory information, focus attention, and form mental representations of the world. In other words, the mechanistic transformations that happen within our brain during brain processes. However, the hard problem of consciousness, a term coined by philosopher David Chalmers, remains unanswered (2). The true challenge of the hard problem of consciousness lies in explaining phenomenal consciousness: how do seemingly unconscious pieces of matter, such as neurons, give rise to the creation of consciousness and subjective experience?

The first issue when tackling this question comes from its definition. The term consciousness remains laced with some ambiguity as it can refer concomitantly to the existence of awareness, state of wakefulness, self-consciousness, brain connectivity and, to some researchers, even as something that is beyond the neural processes that arise from the material (3). Although there is no consensus, we can infer an implicit definition of consciousness from the way in which modern research is being conducted.

“There is no consensus about how it is generated, or how best to approach the question, but all investigations start with the incontrovertible premise that consciousness comes about from the action of the brain (5)”.

Indeed, contemporary neuroscience primarily approaches consciousness research through the search for Neural Correlates of Consciousness (NCCs), the minimal set of neuronal mechanisms which together are sufficient for the emergence of a conscious experience (4). This was quite a breakthrough at the time, finally allowing neuroscientists to focus on identifying the physical manifestations of consciousness without facing funding obstacles or challenges related to the until then controversial subject of the first-person perspective (5). Therefore, since 1990, a new field within neuroscience was established and sought to explain the unexplainable through functional, developmental and neuronal studies, assessment of brain temporal dynamics and studying the effects of pathologies or altered states of consciousness.

A significant part of NCC research involves studying brain activity differences between conscious and unconscious states, such as awake vs. asleep or alert vs. anaesthetised, and during perceptual tasks like the Visual Masking Paradigm, where a brief target stimulus is followed or preceded by a masking stimulus (such as random patterns, other images) to disrupt the target's perception or processing, therefore manipulating the awareness of the stimulus (6). Techniques like Encephalogram, Magnetoencephalogram and Functional Magnetic Resonance Imaging are used to measure brain oscillations and large-scale connectivity, isolating neural signatures linked to the “aware” and “unaware” conditions (7).

The first problem with this type of research is that it equates consciousness to perception. Even if we could take perception as a good proxy for awareness (the state of being conscious of and able to perceive or recognize internal or external stimuli), awareness remains just a fraction of the phenomenon of consciousness (3).

Additionally, it also means consciousness is studied as a binary process, either conscious or unconscious, despite evidence for the existence of intermediate stages, where individuals might not be fully conscious but can still have some degree of awareness of certain aspects of a stimulus. Such is the case of Disorders of Consciousness, with conditions ranging from vegetative state, with an absence of awareness, despite physical arousal, to the minimally conscious state, where awareness is minimal (8).

However, the most important limitation of the search for correlates is that they reveal where consciousness happens but not how: great technological advances have allowed us to know which brain areas are activated during conscious experience, but we don’t know what it is about that activity that produces it.

“Instead of worrying at the so-called hard problem of how conscious experiences could ever arise from mere matter, neuroscientists could get on with looking for brain regions or processes that reliably correlated with particular conscious experiences, or with being conscious at all.“ (9)

As pointed out by Chalmers, in this top-down approach scientists observe behaviours or subjective reports of consciousness and try to correlate them with brain activity, meaning that while it’s possible to identify neural correlates, they aren’t necessarily closer to understanding the mechanisms or principles that make consciousness possible (10).

This begs the question: what are then alternative ways to study consciousness?

In regards to going beyond pure materialistic - thus reductive - measures, more efforts have been going into incorporating the subjective experience further. Researchers, notably Francisco Varela, have called for collaboration with participants to report their subjective experiences during experiments. By

aligning first-person reports with neural data, researchers aim to bridge the gap between subjective experience and objective brain processes. This approach should give glimpses into patients' inner experiences, which can then be correlated with brain activity (11).

Psychedelics have also been suggested to provide unique insights into the nature of consciousness, due to their capacity to produce changes in conscious experience of healthy patients (12). Through the induction of deeply altered states of consciousness, it is possible to study important shifts in awareness, such as unusual changes in perception, emotion, and thought processes compared to what is considered normal or typical during ordinary waking consciousness (13). Furthermore, psychedelic experiences impact one's sense of self, sometimes leading to a phenomenon where the usual boundaries of self-awareness blur (known as ego dissolution), or to profound changes in self-consciousness (or self-transcendent experiences) (14).

Still, while psychedelics can be used to study their effects on consciousness, the idea that psychedelics can be used to explain the hard problem of consciousness seems unlikely: the fact that we observe altered states of consciousness doesn't tell us anything about how they are generated.

Finally, Artificial Intelligence (AI) is said to be a promising tool to solve this question (15). If we can develop an algorithm where consciousness either does or does not emerge based on how components are structured and interact, it would provide a powerful way to test and refine theories about the conditions under which consciousness arises.

However, knowing the ingredients for consciousness doesn't automatically reveal the recipe. With AI it might be possible to move from mere correlation to the realm of causation because subtracting and adding elements becomes a lot easier, but the big how remains, as once again it wouldn't explain how this subjective experience arises.

Finally, the most important question is: would we even be able to tell if AI is truly conscious or just mimicking it? An AI might process information and act like a conscious being, but that doesn't prove it experiences or understands its actions. Even if we used a precise and extensive list of indicative properties, they usually still start with the premise that "consciousness in AI is best assessed by drawing on neuroscientific theories of consciousness", going back to the initial issue of reductionism (16).

This raises the critical question of whether science, as it is currently practised, is even capable of answering the hard problem of consciousness. If it is indeed a problem of definition and conceptualisation, then researchers may have been looking for the wrong thing all along. So far, the dominant perspective of consciousness is a materialistic one, which conceives phenomenal consciousness as identical to brain states, or a dualistic one, which sees it as completely separate from matter, dissociated from brain states (9), (15), (17).

A different perspective that has been proposed to direct the future of consciousness research is monism, according to which consciousness is present in all matter, even at the smallest scales (18). As such, all aspects of reality stem from a unified source rather than two or more distinct types of substances (such as "mind" and "matter" in dualism). According to this theory, there would be no point in explaining how neurons come together to give rise to consciousness, as it's an intrinsic part of matter. This view often intersects with quantum physics, suggesting that if consciousness is treated as a fundamental aspect of matter, it could serve as a unifying principle, bridging the gap between subjective experience and objective reality. As a result of this, we would have to rethink the way we perceive matter, and consequently, neurons: they would no longer be mere pieces of matter, but conscious entities on their own.

We currently don't possess any instrument or method that is capable of assessing consciousness as proposed here. It will be a long time before we can conceive them, and an even longer time before they are created.

Besides this basic verifiability issue, changing the way we see matter would also create a whole new set of problems and questions, such as new perspectives of brain function, but it could also resolve very old neuroscientific disputes, such as where and how memory is encoded or the mind-body problem.

To fully explore these possibilities, however, it would be necessary to have biological scientists and physicists working closely together beyond the separative boundaries between different fields. The very basic concepts on which science relies would be revisited: if matter is indeed conscious, then the line between living and non-living becomes a lot less rigid as well. This would lead to the uprooting of the old Cartesian perspective of Science and pave the way for a new era of Science.

Finally, even though the study of the mechanistic aspects of consciousness is important, I believe that in order to truly understand the origin of such an elusive phenomenon we need to move on from an overly materialistic perspective of natural processes. The hard problem of consciousness will persist for as long as science continues to ignore it, attached to the way things have been in the past, despite the fact that every century or so there is an important paradigm shift which completely revolutionises the way we perceive the world. To understand consciousness, we require the development of a new, unique methodology, unrestricted to neuroscience, opening the doors to a complete shift of perspectives which will probably defy the current scientific paradigm, but that's exactly what good science is all about.

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Gut Feelings: The Microbiota's Influence on Parkinson's Disease Progression

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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.

"The gut is the engine of the body, and the mind follows." — Dr. Michael Ruscio

For years medical science has pointed at the brain as the central player in neurodegenerative diseases, such as Parkinson's disease (PD). However, recent studies show a profound connection between the gut microbiota and neurological healthcare, suggesting that the gut—described as our "second brain"—may hold the key to understanding the onset of PD. Interestingly, it emerged that our intestinal flora could be influencing PD development from disease onset to symptom severity. As we delve into this complex relationship, it becomes increasingly clear that the gut is not merely a passive player, but it can be a key factor that might help researchers to solve the complex Parkinson's puzzle.

After Alzheimer's disease, PD is the second most common neurodegenerative disease worldwide, characterized by motor symptoms such as bradykinesia (slowness of movements), muscle rigidity, postural instability and tremor (1). Hallmark of PD is the degeneration of the dopaminergic neurons of the substantia nigra (SN) and the spreading of alpha-synuclein enriched Lewy Bodies (LB) to other cortical and subcortical areas (1). Consequently, to the breakdown of the SN, more precisely within an area called pars compacta, the level of dopamine decrease leading to an imbalance in the nigrostriatal pathway, resulting in the development of the previously mentioned motor symptoms (1, 2). However, motor symptoms are not the only features that characterize the disease. Anosmia and autonomic nervous system dysfunctions are among the most common abnormalities in Parkinsonian patients (3). Of particular relevance are the gastrointestinal symptoms that manifest in the prodromal stages of the disease, suggesting a more prominent role of the intestinal microbiota, which warrants special attention.

Defined by Michael D. Gershon as our "second brain", the gut shows a diverse flora composed of bacteria, fungi, and archaea, collectively known as the intestinal microbiome. This microbiome performs essential functions, including the maintenance of metabolic homeostasis, vitamin synthesis, drug metabolism, and the development of the immune system (4). Gut dysbiosis has been associated to a large number of pathological conditions, such as inflammatory bowel disease (IBD), Alzheimer's

disease (AD) and obesity. Furthermore, chronic dysbiosis might lead to the development of low-grade inflammation, increased oxidative stress, cellular degeneration, and disturbance of the blood-brain barrier (5). Those features also characterize the progression of PD, thus suggesting a possible link between microbiota alterations and the predisposition to develop the disease. To further support this hypothesis, several analysis on PD patient's microbiota has been performed, showing a different composition compared to healthy groups (5).

In 2007, Braak et al., proposed a dual-hit hypothesis assessing that the disease starts and spreads from two routes: nasal, by anterograde transport to the temporal lobe; and gastric, through the vagus nerve (6). PD is then described as a prion-like disease, having a pathogen (bacterial or viral) triggering a response that leads to a Lewy pathology affecting the olfactory and gastrointestinal system (GI). Focusing only on the GI system, the key point of Braak's theory is that inclusions of alpha-synuclein moved from the enteric nervous system (ENS) to the CNS via the vagus nerve and dorsal motor nucleus of vagus within the medulla oblongata. Braak also described six stages of the disease, and stages 1 and 2 are the ones affecting the ENS and they include symptoms like constipation, dysphagia, early satiety, bloating, and non-specific abdominal pain (Tab.1) (5,6).

GIT Symptom	Brief Description in PD
Constipation	Reduced GI motility, early sign of PD (up to 24 years prior); raises risk of PD. Complications include bowel perforation and megacolon.
Defecatory Difficulties	Muscle incoordination leads to ineffective elimination and fecal incontinence.
Inflammatory Bowel Disease (IBD)	Higher PD risk in IBD patients, linked to the LRRK2 gene.
Early Satiety & Bloating	Due to delayed gastric emptying and intestinal dysmotility, affecting L-Dopa absorption and causing bloating/small intestine bacterial overgrowth (SIBO).
Dysphagia	Affects 80% of PD patients, causing swallowing difficulties that lead to malnutrition and aspiration pneumonia.
Hypersalivation	Caused by reduced swallowing frequency, leading to drooling and higher risk of respiratory infections.

It is well known that the environment impacts the disease's development. Exposure to pesticides and herbicides as well as to industrial solvents and heavy metals enhances the risk of developing PD. Interestingly, several studies have highlighted the effect of some compounds and nutrients that might trigger or have a neuroprotective effect on PD due to their impact on gut microbiota (7). Here table 2 summarises some of them and their impact on PD (6).

Dietary Component	Impact on PD
Caffeine	Inversely linked to PD risk; may stimulate dopamine activity through A2A receptors, improving motor symptoms. Caffeine also enhances L-dopa's effects, increasing dopamine levels.
Tea	Potential neuroprotective effects, especially non-black tea. Polyphenols (e.g., EGCG) and theanine may reduce oxidative stress and inflammation, improving dopamine levels and brain circulation.
Dairy	Higher milk consumption is associated with increased PD risk, with studies showing a 17% higher PD risk for every 200g/day of milk. However, low uric acid levels due to casein in dairy might contribute to higher risk.
Fruit & Vegetables	High intake of antioxidants reduces PD risk. The Mediterranean Diet (MD), rich in vegetables, fruits, olive oil, and fish, has shown beneficial effects on PD prevention and neurological health.
Vitamins	B12 deficiency linked to PD; B6 and B9 supplementation may decrease risk. Vitamin D may help with motor symptoms, and higher intake of Vitamin E could reduce PD risk. Vitamin C is neuroprotective, but its link to PD is unclear.
Fats	High animal fat intake may increase PD risk, especially arachidonic acid and cholesterol. Omega-3 polyunsaturated fatty acids (PUFAs) may reduce PD risk by providing neuroprotective effects. Ketogenic diets have shown some benefit in animal and clinical trials.
Carbohydrates	Carbohydrates may influence dopamine production, with high glycemic index foods possibly increasing dopamine. While a low-fat, high-carbohydrate diet improved symptom, the relationship between carbohydrate intake and PD risk is not clinically significant. Diabetes medication (e.g., exenatide) might offer neuroprotection in PD.

This evidence might point out the fact that a balanced diet can play a key role in preventing Parkinson's disease or at least delaying its onset. Especially, Mediterranean diet shows very positive effects thanks to its variety of foods and micronutrients, beneficial for preventing the onset of inflammatory processes.

An imbalanced intake of macro- and micronutrients can have detrimental effects on our gut, leading to conditions such as dysbiosis, which is characterized by an alteration in the microbial composition of the gut, promoting the growth of pathogenic bacterial species over commensal ones (8). Different studies have consistently shown reduced microbial diversity in PD patients compared to healthy controls, highlighting significant differences in microbial composition. Furthermore, a 2021 meta-analysis by Romano et al reinforced these findings, identifying distinct gut microbiota profiles in PD (9). Altered microbial compositions are observed in both early and advanced stages of PD, including an overgrowth of coliform bacteria and elevated urinary indican levels—markers of dysbiosis—pointing to a potential role of the gut microbiota in PD pathogenesis.

The following table summarizes the bacterial taxa that have been consistently identified in studies as exhibiting significant differences in abundance between Parkinson's disease patients and healthy control (Tab 3)(9).

Bacteria	Symptoms Associated with PD	Role
Ralstonia	Increased levels of pro-inflammatory gram-negative bacteria.	Non-protective (associated with symptom worsening)
Eubacterium (E. eligens, E. rectale, E. hallii)	Higher UPDRS scores, worsening disease state.	Non-protective (associated with symptom worsening)
Enterobacteriaceae	Postural instability and gait disturbances.	Non-protective (associated with symptom worsening)
Prevotella	Decreased mucin proteins, increased intestinal permeability, potential early biomarker for PD.	Protective (associated with anti-inflammatory effects and improved gut health)
Lactobacillus	Altered ghrelin secretion, frequent constipation.	Non-protective (associated with gastrointestinal symptoms like constipation)
Blautia	Decreased anti-inflammatory species, reduced butyrate levels.	Non-protective (associated with reduced butyrate production and worsening GI symptoms)
Coprococcus	Decreased anti-inflammatory species, reduced butyrate levels.	Non-protective (associated with reduced butyrate production and worsening GI symptoms)
Akkermansia	Possible increase in intestinal permeability ("leaky gut") with inflammatory effects.	Non-protective (associated with higher intestinal permeability and inflammation)
Helicobacter pylori	Worsening of muscle rigidity, decreased walking speed, interference with levodopa absorption.	Non-protective (associated with worsening motor symptoms and interference with medication absorption)

To conclude, growing evidence supports a significant relationship between gut microbiota and Parkinson's disease (PD). The influence of the gut appears to be more substantial than previously thought, with Braak's hypothesis offering a promising explanation for the gastrointestinal tract's role in PD pathophysiology. This theory is further supported by various pathological studies investigating alpha-synuclein and other neuropathological changes throughout disease progression. Clinical research has also provided additional evidence of gastrointestinal symptoms, dietary impacts, as well as shifts in gut microbiota levels in PD patients. The range of gastrointestinal symptoms and conditions observed in PD patients may reflect the underlying pathophysiological processes of the disease. Early recognition of these symptoms could be crucial for early diagnosis and more effective holistic management. However, it is essential to note that the gut microbiota may not be involved in the prodromal phase of all PD cases, suggesting that a more focused systemic approach is necessary. Furthermore, the role of gut symptoms in early-stage PD is still unclear, but identifying these signs early could offer insights into the initial stages of disease development. Current evidence emphasizes the importance of diet in PD development and progression. The Mediterranean diet (MD), for example, may also play a pivotal role in PD research, with its well-established health benefits. Nutritional therapies could not only reduce PD risk but also alleviate symptom severity. When combined with existing medications, dietary approaches may enhance bioavailability and pharmacological effects. However, more research is needed to explore the impact of diet on an individual level, as most current findings are based on epidemiological studies or meta-analyses. In summary, the role of gut microbiota in PD is increasingly recognized as significant. Dysbiosis in PD patients is linked to gastrointestinal diseases and Parkinsonian features, with Lactobacillus and Prevotellaceae being two bacterial taxa of particular interest. Probiotic treatments and faecal transplants involving these species may offer promising future therapeutic avenues. This evidence suggests that exploring the role of nutrition on gut microbiota in PD patients could provide valuable insights into personalized treatments that would offer hope for better management and potentially transform the future of PD care. In sum, taking control of one's diet it is not just a matter of weight control, but a way to preserve the health and a powerful ally in the battle against Parkinson's disease!

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Women's Voices: Inspiring the Neuroscientist Community

Enrica Montalban

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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 **Enrica Montalban**, an Italian postdoc student working at Nutrineuro. The research interests of Enrica include reward and dopamine in the context of psychiatric disorders. She has been recently awarded with the Marian Diamond Prize, aiming to highlight women neuroscientists at the post-doctoral period.

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

Enrica Montalban: I am currently a post-doc at the NutriNeuro laboratory in the NutriPsy team. My academic career started at the University of Rome "La Sapienza", where I obtained my master's degree. Having collected encouraging results during my internship, I decided to pursue my research before starting a PhD. I hence secured a grant and completed my project at the European Brain Research Institute, in Rome. In 2012, I obtained a Marie Skłodowska-Curie Initial training network fellowship and started, under the supervision of Dr. Girault, a joint PhD between the Institut du Fer à Moulin in Paris and the Prof. Greengard's laboratory at Rockefeller University (New York). The aim of my project was to identify the molecular mechanisms underlying long-term adaptations of dopamine sensitive neurons of the striatum to reward processing-related physiological and pathological states. As during my PhD I developed a strong interest in the neurobiological bases linking reward alterations to eating disorders, in 2018 – thanks to the obtention of post-doctoral fellowship from the Fondation pour la Recherche Médicale- I joined the laboratory of Dr. Luquet with the aim of understanding the

interactions between metabolic and reward circuits in the control of feeding. I moved to Bordeaux in 2022.

Sara Carracedo: Could you tell us more about your current research focus?

Enrica Montalban: Following my first postdoc, I developed a strong interest in the interaction between nutrition and inflammation in the vulnerability to psychiatric diseases related to a dysregulation of the reward system, and in particular major depression. In May 2022, I therefore decided to join the NutriNeuro laboratory headed by Dr. Capuron. Within her group, I proposed a translational research project, aiming at exploring the hypothesis that cerebral astrogliosis induced by adiposity-related inflammation is directly responsible for a disturbance in dopamine transmission, thus participating to the onset of depressive symptoms such as loss of motivation.

I am therefore currently conducting a translational project exploring the link between astrocytes and dopamine transmission using chemogenetics to selectively manipulate astrocytes and in vivo imaging coupled with dopamine sensors in behaving animals. In parallel I am using dopamine radioligands coupled to positron emission tomography (PET) to assess dopamine levels in relation with depressive symptomatology in obese patients.

Sara Carracedo: You received the Marian Diamond Award for academic excellence, an initiative of the Bordeaux Neurocampus Parity Committee. Can you tell us about the academic achievements or recognitions you have received during your PhD?

Enrica Montalban: For my PhD I have had the chance to be selected for a Marie Skłodowska-Curie Initial training network fellowship (NPLAST). The fellowship covered almost all of my PhD and it has been a unique chance to interact very early in my career with already established and talented scientists. My PhD work was then central for obtaining a post-doctoral fellowship from the Fondation pour la Recherche Médicale. My work has also been awarded by the Fondation de Treilles, from which I obtained the "Young Researcher Award".

Sara Carracedo: You are currently part of the Neurocampus Parity Committee, what motivated you to join this group? Which initiatives from this committee do you think are particularly important?

Enrica Montalban: During my academic journey I understood that recognizing unequal treatment is not always easy. The principal motivation(s) that I have in participating to the parity committee is to make people more aware of gender biases and to be involved in the effort of identifying and preventing unequal behaviour at all levels, not only within the scientific system, but also regarding our everyday life in the lab. Diversity is crucial to our society and to the progress of science, participating in this committee is a great way to contribute to emphasizing it.

I very much appreciate the work that the NeuroPIC has been doing. Data regarding gender bias are being collected and analyzed with scientific rigor through well-designed surveys. This work is of particular importance as it might open the eyes of scientists in the community through actual, undeniable numbers. This is a crucial step to make the community face the problem with objectivity and a steppingstone to tackle the causes of inequality.

Sara Carracedo: How do you balance the demands of research and personal life? Do you think this balance is more challenging for women in academia?

Enrica Montalban: I have always been very passionate with my research projects, therefore for a long time working hard was just a part of my "personal life", in particular in the early stage of my career. I guess that one of the keys is to try to understand that putting some distance between personal life and research is beneficial even from a professional perspective. It is always more productive to think with a fresh mind. Keeping a balance can be complicated and I do think that it is way more challenging for women. I am experiencing this even more now, as a senior post-doc in a critical point of her career and as a mother of a 16-month-old child. While my situation is particularly understandable and accepted by our society, I do think that motherhood is only one of the scenarios in which a woman will struggle more to keep a balance. For example, we can still come across stories in which a woman needs to produce more in order to demonstrate her professional value. Which of course will impact on her personal life.

Sara Carracedo: What advice would you give to other early career women in neuroscience who might be facing gender bias or discrimination?

Enrica Montalban: My first advice would be to keep doing their research the best they can. Good research will be recognized, independently from the gender. I also advise to try to have an honest and trustworthy network of scientists to refer to when doubting of research projects or career ambitions. It is also crucial to be intransigent against any form of gender bias and discrimination that we or others can be facing. This implies to be able to detect them, starting from the language and the way of interacting with women. Although academia still has room for improvement, the system is changing in the good direction and could become an example for society. It is therefore crucial that everyone feels concerned and participates in this challenge by identifying the everyday biases and discriminations, and actively acts against them.

Is your brain in your hands?

Interview with Silvia Bunge

Juan García-Ruiz[1]
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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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There is a great cliché that says that we are all the same. And another one that says that each person is unique. But what does biology say about this? If we take as an example the genome, which is the set of DNA in our whole organism, we can understand these statements a little better. If you compare the genome of two individuals of our species, you will find that they are 99.6% identical and 0.4% different. With these figures, it is not unreasonable to say that we are all the same. But what about the 0.4%? This percentage is not insignificant on the scale of 3,000,000,000,000 nucleotides and more than two tens of thousands of genes. This genetic variability - along with many other factors such as lifestyle, social context, and diet - is what makes us unique.

And does all this have an impact on our lives? How do these genetic similarities and differences manifest? The truth is that many of the genomic variations have no known effect on the functioning of the genome. However, a small subset of these variations is sufficient to give rise to some of our differences. From the more noticeable ones, such as the color of our eyes, to the less obvious ones such as our cognition.

But let's not be reductionist. Genes are not everything. In fact, some studies suggest that the influence of genes on our cognition is more important the higher the socioeconomic status. It is becoming increasingly clear that

understanding biology should not involve taking sides in the hereditary versus acquired stupid war. Let's accept reality as it is: something extremely complex. In the end, the final message is the same: we are what we think, and our thinking is what unites us as human beings. But it is also what separates us. Cognition is both a common denominator and a dividing line.

I would like to tell you much more about the development of our cognition. But it turns out that, unlike Silvia Bunge, I do not specialize in high-level cognitive functions. Nor do I devote my life to understanding how educational experiences and our family environment can modulate our cognition. Luckily, I had the pleasure of interviewing her. Who is Silvia Bunge? This renowned researcher was born in Montreal, Canada. She completed a bachelor's degree in biology at Yale University. Then she went to grad school at Stanford, where she started doing cognitive neuroscience research. Then she went to MIT for a postdoc and had her first faculty position in psychology at University of California Davis. Her current position in psychology and neuroscience is at UC Berkeley. She runs a cognition lab where she studies higher level cognitive functions like reasoning and goal directed behavior, as well as memory. She does this in both healthy typically developing adults, as well as in children and adolescents. She is also interested in brain plasticity and in how home and educational experiences can modulate our behavior.

Juan García Ruiz: What goes first, the brain or the cognition?

Silvia Bunge: My father was a philosopher of science, and he wrote about the mind body problem. So exactly this, how does the brain support cognition, and I very much subscribe to his ideas. He was a monist, so he thought that the brain is what supports cognition and there's nothing else. But in his conception, he considered that there are levels of complexity that come to play at those different levels. So you cannot reduce cognition down to molecular interactions. But from molecular interactions you get the emergence of more complex systems at the cellular level, then at the system level, and then you have the final level of complexity that is cognition. The same way the gut produces digestion, the brain produces cognition.

JGR: If I had no access to education at all, how different would my brain be?

SB: There's been very little research on non-weird populations. Most of the research is based on the population of Western, educated, industrialized, rich, democratic countries. What we do know from behavioral research, is that we see the same behavioral functions that are appearing during development. Numeracy is a good example of that. Kids acquire number systems in the same way regardless of their number knowledge. In a society where people don't even talk about numbers, you still can see some understanding of number concepts that increase in the same way but maybe just develop on a different timeframe. And the same goes for motor development and language. There are some cultures where people don't speak to you directly as a child and you learn maybe more slowly. But you ultimately get there. Our brains are very similar. Whatever experiences we are getting, we are slightly tweaking the basic template.

JGR: So even if I hadn't access to education, my cognition in general terms wouldn't be that different from that of someone who did have an education.

SB: Absolutely. But you would not develop other features. There's research on, for example, people who never learned to read. The brain area involved in the transformation of visual words to sounds is not as developed as in someone who did learn to read, even though language is developed anyway.

JGR: But cognition is also constituted of building blocks, so if we don't acquire certain cognitive abilities, we could lack other skills consequently, right? I guess there's even some degree of emergence in cognition in a way that a few more simple skills can give rise to a complex cognitive ability.

SB: Yes, of course. If you don't learn to read, for instance, everything is going to snowball from there: you are not going to read advanced texts, you are not going to develop critical thinking skills and other high-level mental processes.

JGR: You conduct a study involving children and teenagers from 6 to 19 years old to track the changes in their brain that allow the emergence of high-level mental processes high level. What are the conclusions of this study so far?

SB: Some of our most recent findings suggest that there are individual differences in anatomy that are going to influence the trajectory of the brain. Lately, we've been looking at the sulci, so the wrinkles in the brain. These form quite late in development, and we think that they're fairly sensitive to the environment. We found that whether you do or don't have specific sulci, or what they look like, does predict the growth of your reasoning over time. There are some anatomical differences between people that influence what is or what isn't possible for the developing brain. Apart from that, one thing we've looked at closely is the development of the very front of the brain, the rostral lateral prefrontal cortex, and its connections to parietal cortex. We've found that strengthening of these connections in terms of white matter and in terms of functional coupling are both good predictors of reasoning development.

JGR: Can you tell me more about this relationship between the sulci and cognition with an example?

SB: I've been obsessed with a rostral lateral prefrontal cortex for 15 years. Recently, students working with Professor Kevin Weiner and me found that some people have a specific sulcus in this region, and some people don't. It turns out that the people who do have it have around 30% higher reasoning ability. We found this in kids and adolescents and we published that. And now we just found it in a separate sample of adults as well. We think that there are probably bidirectional relationships between sulci formation and white matter development. The sulci form when the white matter tracts are forming and that creates physical tension in the brain. In addition, in some sulci the white matter is inserted into the cortex, and those short-range connections could reflect more local processing of information. Beyond that, the depth of different sulci in the prefrontal cortex is associated with reasoning as well. And concerning the cortical gray matter thickness within the sulci we do find changes associated with the development of reasoning.

JGR: Concerning higher cognition, what are the most exciting findings you have found?

SB: We did a series of studies looking at whether reasoning ability could be trained. We were interested in looking at a real-world example of that. We went with this course, that's very common here in the United States, to prepare you to get to law school. The reason we picked this is because it's all focused on critical thinking and abstract reasoning. We wanted to know whether studying for this exam over a period of time like three months, could strengthen this reasoning network in the brain. And if this improvement could be transferred to other tests.

We published a series of papers showing improvements on completely different reasoning tasks. In the law school admission tests the problems to solve are all verbal. But then we also found improvements in nonverbal visual reasoning tests. We also showed increases in white matter in prefrontal and parietal cortices and increased functional coupling between these regions. With fMRI, we showed decreased activation of a region of the prefrontal cortex that is associated with difficult decision making.

JGR: What do we know about home environment and the development of higher condition?

SB: A lot of people have been looking at this in the context of poverty. If you look at the papers closely, on average, people who live in poverty have lower cognitive skills. But there's a huge variability across the socio-economic spectrum. In our work, we found something that was unexpected: we have seen in typically developing kids an interesting brain – behavior relationship. By typically developing I mean, the typical samples who come into the laboratory, which are usually middle – upper class and normal schooling because they are more prone to participate in this kind of research. So most of what we know about brain development comes from these kids. In that work, there's a pattern of connectivity between two brain networks, that is associated with better cognitive ability. One of the brain networks is involved in focused task performance, and we call this the executive function network. The other one is related with internally guided thought, which is involved in introspection about yourself, like when you are thinking about the past or the future and you are distracted from a goal. What others have found is that the more dissociated these networks are, the better the cognition. This makes sense because the more you are focused on a goal, the more you want to suppress any kind of internal distraction.

But what is really surprising is that my former student Monica Ellwood-Lowe found that kids in poverty show almost the opposite relationship. It's really interesting, because in these cases there seems to be an environmental pressure that leads the brain to develop in a slightly different way that confers resilience in these

kids. Somehow, they get to the same cognitive outcomes through a different mechanism. We don't know the underlying mechanism. We think it relates to vigilance. And we have some evidence of this. There's this other brain network that's involved in heightened awareness. And there's a dissociation of this network from the other two networks in kids in poverty that could maybe explain the previous finding.

JGR: What are the networks you just referred to?

SB: The one involved in task goals is the lateral frontal parietal network. The one involved in the introspection, we call it the default mode network, and it involves regions located in the middle of the brain. Finally, the regions involved in alerting to some sort of threat or challenge, which are part of the so-called singular particular network, include the anterior cingulate and the anterior insula.

JGR: What other environmental factors could have an impact on cognition apart from the economic level?

SB: In one of our studies, we were looking at various environmental variables. Some of the ones that came into play were the danger level in the neighborhood in terms of crime rate, the type and the quality of school they go to, etc. To take the example of the danger level, we showed that the higher the crime rate, the more different these high performing kids were from the typical sample. These relationships are not only present for abstract cognitive abilities, but also for grades and for attention problems that are reported by parents.

JGR: Could some factors account for positive effects on brain and cognitive development?

SB: Of course. First of all, kids in poverty are learning other things. And there may not be things that we are valuing, or even studying. They may be learning to be more self-reliant or creative, or to process more information. There are some ideas around that. Then more generally, better schooling has been associated with better reasoning ability. We have a review paper on that. Then there is also caregiving, which can be a very important buffer against early adversity.

JGR: Considering the relevance of a proper schooling for adequate cognitive development, are there things that could be implemented to improve the schooling conditions of kids in poverty?

SB: I think the most important thing is to pay teachers a good wage so that most educated teachers work in these schools where kids in poverty are studying. Any kind of quick fixes like a cognitive intervention is not going to have a long-term impact. In the US, they have invested a lot in early childhood. And that's great, but you can't stop there. The brain continues to change and is still sensitive to input, so what we need is high quality education at all stages. Beyond schooling, at an individual level, there are three other important factors that are related to physical health. We can contribute to our cognitive health if we take good care of our sleep, nutrition and exercise. Kids in poverty have access to worse nutrition and get less sleep. And I think sleep especially can make a great difference.

JGR: Is there a book you would like to recommend to the readers?

SB: The book that really got me started on neuroscience was *The Man who Mistook his Wife for a Hat*, by Oliver Sacks. It was the most influential for me. My mind kind of exploded when I read it as an 18-year-old.

JGR: Do you have a final message for the readers?

SB: Your brain is in your hands. What you do repeatedly is going to influence your outcomes. You shouldn't be afraid to try new things. Your brain is plastic, and you can do things you didn't think you could do. It's important to maintain your cognitive ability with new challenges, without forgetting to maintain your physical health as well.

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Toshiko Sekijima, 1st year PhD student at Nutrineuro

Simon Lecomte, 3rd year PhD student at the IINS

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Editorial board

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.

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.

Aude Verboven

Aude, directly coming from Bordeaux, is a PhD student at the Neurodegeneratives Diseases Institute (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.

Sara Carracedo

Born in Spain, Sara is a PhD student at the 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 pursuing a PhD at Nutrineuro, focusing on the protective role of gut microbiota-derived indoles in inflammation and psychiatric health. 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. Beyond her research, Toshiko is passionate about scientific illustration (IG @toshi.co).

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).

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