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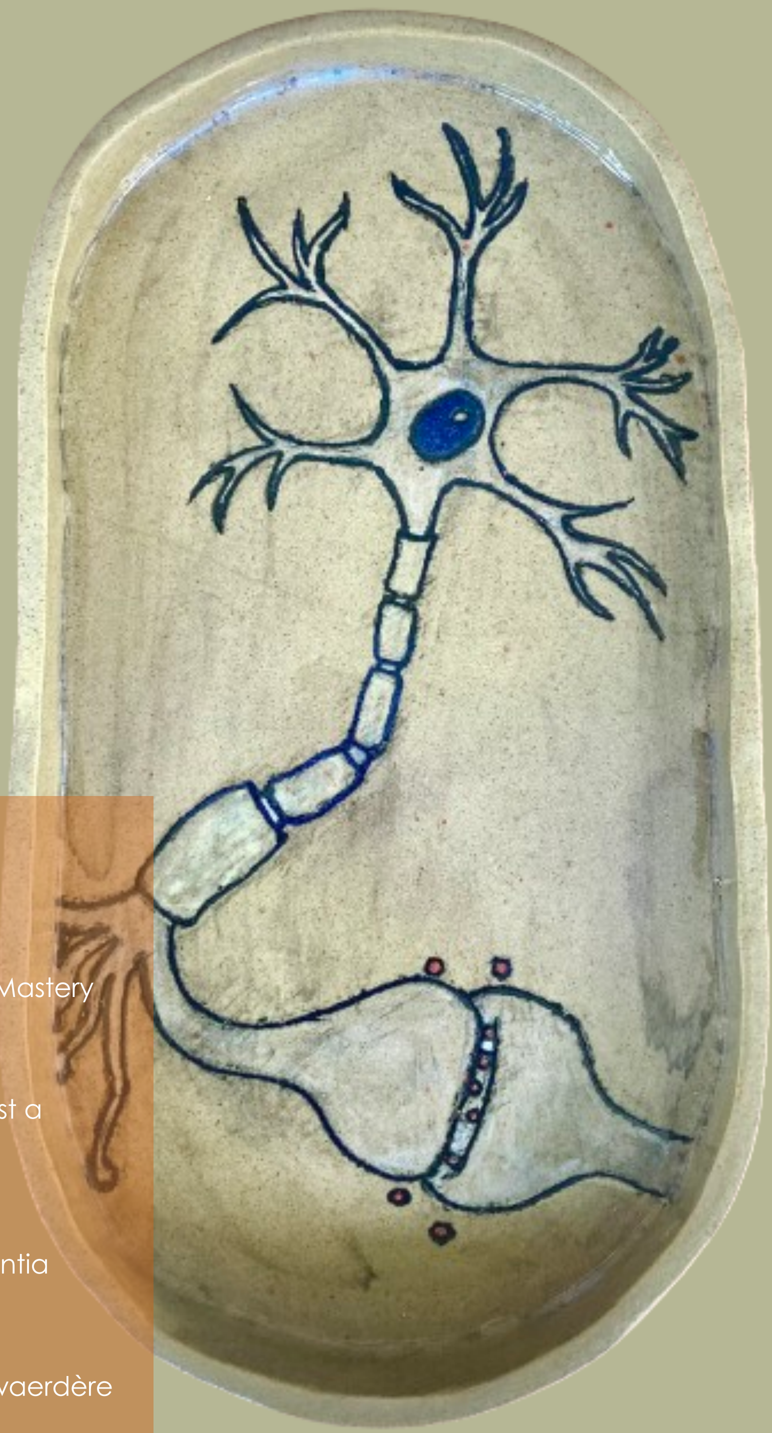

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All authors take responsibility for the content of their publication.

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UNLOCKING ROBOTIC MASTERY:

Learning from Humans on how to learn

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Born in Punjab (Pakistan), Muneeba holds a bachelor's degree in Computer Sciences from FAST NUCES Islamabad University. She is currently doing a Master's in neurosciences from the University of Bordeaux. Her research interests are focused on computational sciences and brain computer interface. Outside the masters, she will be part of the organization team of the Brain hack school.

Abstract

The quest to imitate human-like intelligence in robots has seen significant advancements in recent years. This article explores the methodologies employed by researchers to imbue robots with the ability to learn autonomously and generalize tasks across various environments. Drawing parallels between human learning mechanisms and robot training strategies, researchers have endeavored to imbue robots with the ability to learn autonomously and generalize tasks across various environments by employing neural networks and deep reinforcement learning

Keywords

Generalizable robotic reward functions, generalizable task learning in robots, single-life robot deployment, artificial neural network, machine learning, brain-inspired models, and brain- inspired learning.

Abbreviations

Convolutional Neural Networks (CNNs)

RObust Autonomous Modulation (ROAM)

Introduction

You might have seen droids in the movie Star Wars, and even if you have not, you might have heard about humanoid robots, intelligent robots, or robots taking over the world. In popular culture, the notion of robots with human-like intelligence, reminiscent of those seen in the Star Wars movies, has intrigued, and sometimes concerned us. In 2010, the idea of imitating intelligence started to seem feasible; artificial neural networks, particularly Convolutional Neural Networks (CNNs), began to demonstrate capabilities akin to human visual perception, notably in object recognition tasks [1]. It could recognize mites within a cropped image and a scooter, even in bad lighting, as shown in figure 1. The object recognition model was indeed directly inspired by the statistical model representation of the biological neural network of the human brain for pattern recognition presented by Fukushima [2] as shown in figure 2.

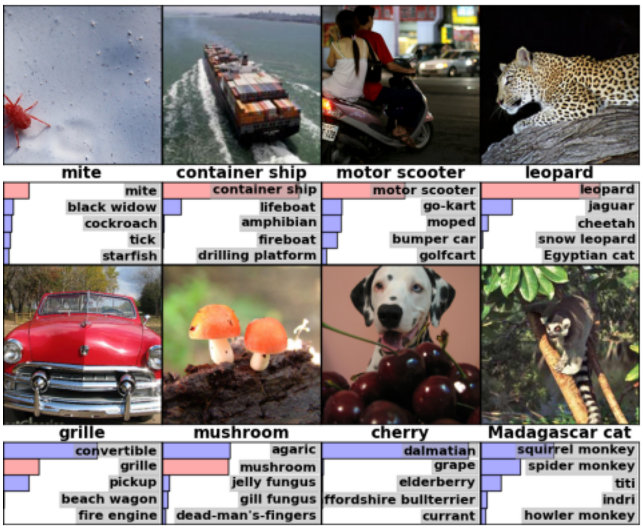

Figure 1. ILSVRC-2010 test images and the five labels with best probabilities [1].

a

b

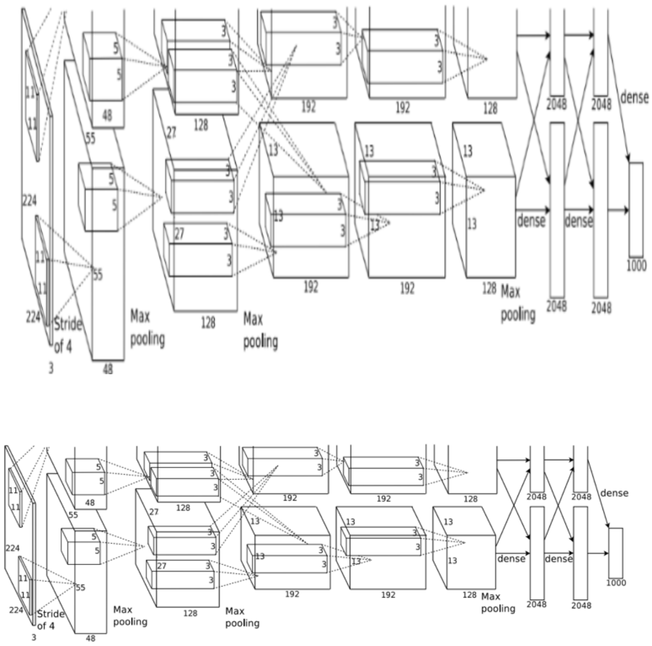

Figure 2. Models Comparison. (a) Architecture of CNN for pattern recognition [1]. (b) Statistical model of biological neural network for pattern recognition [2].

Figure 3. Guided by, from left, Chelsea Finn, Sergey Levine and Pieter Abbeel, Brett (the Berkeley Robot for the Elimination of Tedious Tasks) Credit: Peter Earl McCollough for The New York Times.

With the advancement in technology and processing power, researchers ventured into mimicking human brain cognition [3], such as creativity [4] [5], and generalization [6] [7]. One notable milestone came in 2015 when Chelsea Finn and her team showcased a robot trained to perform tasks with human-like dexterity and adaptability [8], which was at the forefront of the press, including New York Times magazine as shown in figure 4.

The present article provides an account of the work conducted by Chelsea Finn and her team on training robots to acquire generalizable skills through subtle human-inspired methods. Overall, the work underscores the potential of integrating human-inspired approaches into the design and implementation of robotic systems to improve their functionality and performance.

Methods

Articles cited in this review were found using Google Scholar. The following keywords have been used: imagenet classification CNN, neu- ral network visual pattern recognition, deep visuo-motor policies, generalizable robotic re- ward functions, generalizable task learning in robots, and single-life robot deployment.

Results

One of the ways humans learn is by exploring and experimenting. In an experiment by Chelsea Finn and her team, the robot was placed in an environment where it could interact with objects and learn to solve tasks from scratch [8]. Through deep reinforcement learning, the robot gradually figured out the task. The images from robot cameras fed into the neural network and their output torques were directly applied to the robot arm. It is remarkable that the robot could learn autonomously and was embedded end-to-end with a robotic arm. However, a significant challenge emerged: the robot was not learning general-purpose skills that could be ap- plied across various objects or environments. The robot had to start learning from scratch whenever it encountered a new environment, rendering its previous learning ineffective [9].

Recognizing that humans learn from a broad range of data and through exploration, the team allowed the robot to move and collect data on its own in an attempt to address this limitation [10]. While this approach provided some benefits, it generated a large amount of unfiltered data with noise, making labeling the data challenging. Furthermore, human guidance of the robotic arm towards the correct action, akin to guiding a child, also faced limitations as data collected in this manner is often limited in number and time taking [11].

Acknowledging that humans also learn through observation, the researchers pivoted to a new approach [12]. They utilized the” something-something” dataset, a vast collection of video clips showcasing humans performing basic actions with everyday objects. This approach involved two main phases: the training phase and the testing phase. The model comprised an encoder and a binary classifier during the training phase. The encoder transformed videos into simplified representations called embeddings, and the classifier determined whether two videos performed the same task. This combination of encoder and binary classifier, termed DVD, which, when passing two videos, outputs the probability of videos performing the same task or not.

During the testing phase, a model called VMP, previously trained on a comprehensive dataset called” something-something,” was employed. Its role was to anticipate future sequences of actions based on a given image. For example, if shown an image of someone holding a half-open drawer, VMP would suggest potential trajectories such as closing the drawer, opening it further, or moving it back and forth. These predicted trajectories were then compared with human demonstrations through DVD, yielding a score of functional similarity. Whichever trajectory has the highest similarity with the human demo, the robot would perform that action. As a result, the robot was able to place a lid on a bottle or position an object in a pan.

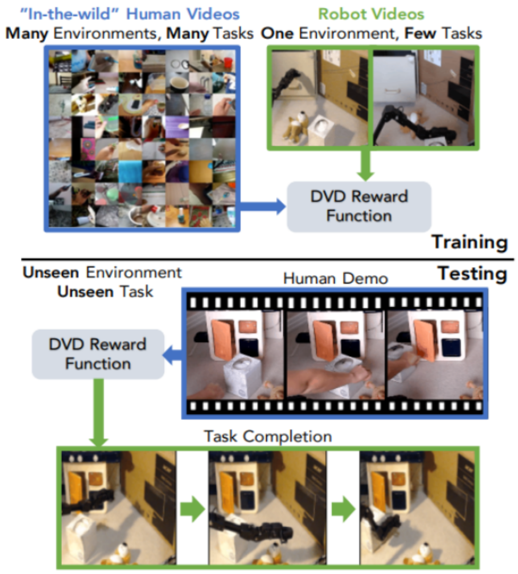

Figure 4. Model architecture depicting training and testing phase

It was rather challenging because it involved maneuvering a spatula with a certain speed and placing an object in the pan. On watching a video of someone opening a drawer, the robot was also able to open the drawer. Although the robot successfully mimicked human actions, it does not know the physics behind it. For example, we might have never encountered a scenario where a heavy metal object ball crashed the glass, but we are still able to predict the outcome.

Currently, the team is working on ROAM (RObust Autonomous Modulation), an innovative approach that enables robots to adapt autonomously to novel scenarios in real time. This approach involves equipping the model with a repertoire of fundamental skills, which are dynamically combined to address new challenges [13]. While ROAM excels in problem-solving, its limitation in providing a deep understanding of the physics governing objects and environments still persists. Nevertheless, it represents a notable shift away from simply imitating behaviors; instead, it fosters a learning process where robots not only replicate but apply learned behaviors to tackle novel problems.

Conclusion

In conclusion, while significant progress has been made in training robots to perform tasks with human-like dexterity and adapt- ability, challenges persist in enabling robots to learn generalizable tasks applicable across diverse environments. Leveraging datasets such as the" something-something" dataset and innovative approaches like ROAM hold promise in addressing these challenges and enhancing robotic autonomy. The fusion of human-inspired methodologies with cutting edge technology holds immense potential for enhancing the functionality and performance of robots in various domains.

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Dance: more than just a movement

A musical journey into hidden corners of our mind

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Forming social bonds and embracing living in communities are one of the most fundamental behavioural characteristics of human nature. We are inherently social creatures, endeavouring to form connections with others (1). In this world marked by racial and cultural diversity, effective communication is the cornerstone of successful social interactions. Despite such important global diversity, there exists a universal language that can break down the cultural barriers and connect us: the language of movement. Movement can enable us to communicate feelings, sometimes even more effectively than words. Our body itself can convey our emotions and intentions (2).

One of the most expressive and complex forms of movement is dance (2). In many societies, it is an integral part of their community. In the West Sepik District of Papua New Guinea, we still can find Umeda people expressing gender roles via the yearly Idā dance, which honors sago palm fertility and symbolizes their endurance amidst both physical and mystical challenges. In Orissa, part of India, since the fifteenth century there has been a tradition where young boys dress as girls and dance to honor Krsna. It is believed that the most effective way of showing devotion is as a female. And in Tanzania, the Gogo community still performs the Cidwanga dance each year to honor and invoke favorable rains and fertility in their ritual practices (3). Certainly, it has been already ingrained in the human condition since ancient times. When you think about the dance, you're likely to associate it with leisure. This is indeed true, synchronized dancing fosters social bonding and gives an impression of interconnectedness. However, dance has held relevance in other areas of life including war dances, various rituals, storytelling, and performance art (4).

Over the centuries, a lot has changed with our approach to dance. For the societies that are more modern, together with the development of technology, some customs vanished, and dance has retained mostly its artistic and entertaining function. For instance, war dancing has taken a form of sport rituals like cheerleading or Haka, historically performed before battles to intimidate opponents, now adopted by New Zealand's national rugby team, the All Blacks, as a pre-match ritual (5). The tradition of dancing to summon the rain or to thank the gods for better crops at harvest time faded. Of course, it continues to be present in some ethnical communities, like Navajo or Hopi tribes from

Southwest region of the United States. They still perform “rainmaking” during drought to summon spirits of the gods to cleanse the earth with rain (6). However, for Western societies this role of dance seems abstract, while weather forecasts are available. Then, what about the entertaining aspect of dancing?

While in many cultures dance remains an integral element of their everyday customs, in others it has been marked by a certain inaccessibility. Among some people, dancing became not a common occurrence, but typically reserved for special moments or events. This division is strongly visible between people from warmer countries, especially Latin people, and people from colder, northern countries. As a Polish woman who moved to Barcelona, I come across people singing or dancing on the streets more frequently than in my home country. This observation got me thinking and made me delve more into the ground of this interesting occurrence. And before you disagree with me by saying that we, after all, dance all the time at the parties or festivals, ask yourself few questions. How many times have you stopped on the street while walking and randomly started dancing alone, or with a stranger? Or when was the last time you tried to dance out the emotions like happiness, sadness, or frustration? Or how many times you were watching dance performance in theatre thinking that you wish you could be on the stage now, but you can’t dance? This perfectly shows that we reduced the dancing aspect to a minimum. We treat it as something that either must be perfect and is reserved for the professionals, or as something we do only when we are in the crowd, which is limiting the aspect of our individual expressiveness.

This problem has been already emphasised by Barbara Mettler, a remarkable dancer and dance educator. Her lifelong work is centered around the belief that dance is a fundamental human need. When she heard someone saying that they wished they could dance, she tended to ask for the reason why they were not doing it. She received answers like: I am not graceful. I don't have ideal body. I am not creative enough. It is too late for me. I am too old (2). Majority of people treats dance like something special, only available for professionals. Many consider it as something for chosen ones and avoid dancing, especially when they didn’t dance in their early childhood. The conviction exists that dancing requires special skills, and there’s a perceived notion of a "correct" and "incorrect" way to execute movements. Certain individuals feel anxious about dancing or being in the presence of others who are dancing –a condition described as chorophobia (7). Personally, I am under the impression that this stigma is only increasing with time. We seem to have forgotten about the importance of the dance. We forgot that it doesn’t always have to be sophisticated, but that it can be simple too. It is the easiest way to express ourselves without words and it is in our nature to dance. Rhythms of the body are critical throughout our life. Movement is the first action of the nervous system, and the correct development of brain and body is through the spontaneous movement of the fetus (8).

The aim of my letter is to loosen up those blockages by showing the positive aspect of dance from the scientific point of view. Additionally showing that it is never too late to start dancing and that learning this at any age can be beneficial. You cannot disagree with me, when we dance, we are happier. The question, however, is: what is really going on in our mind?

First, let’s have a look at dance as a form of physical activity. Obviously, for the reason that physical activity is widely known to improve cognitive functions. Some mechanisms by which exercising achieves these outcomes are through triggering an increase in endorphin levels, the body's natural feel-good hormones. Dance can be considered as a unique form of physical activity. It combines complex movements with aesthetics, music, and carefully choreographed sequences. What is more, it often involves touching, eye contact, and synchronized movement with other individuals. Dancing challenges memory, coordination, and focus, making it a fun way to stay mentally sharp (9). It has positive effects on neuroplasticity, since it involves learning, remembering, and executing complex motor movements, following instructions, and integrating visual and rhythmic movements (10). Indeed, some MRI studies suggested neuroprotective effects of dance, prevention of age-related degeneration of the brain especially responsible for memory functions and increase of resting-state activity in the fronto-temporal areas responsible for maintaining cognitive functions, like memory (9).

Did you know that if you start dancing in adult years, you can decrease the risk of development of certain diseases, especially depression, dementia or even Alzheimer's Disease. In some studies, regarding elder mild cognitive impairment, a beneficial aspect of dance therapy has been shown. One study assessing the effects of a 3-month aerobic dance intervention in older adults with cognitive disfunction revealed significant improvements in white matter integrity of the left hippocampus of the cingulate fasciculus, and the left superior longitudinal fasciculus, which are areas closely associated with memory and cognitive function (9, 10). Another study showed 6 months of practicing aerobic dance can significantly improve executive function. This might be correlated with structural and functional changes in the prefrontal cortex, reflected by the increase of grey matter volume and higher activation in prefrontal regions upon dancing training (10, 12). On the other hand, there are several studies investigating the positive effect of dance in Parkinson's Disease (PD) support. Some research indicates that Argentine tango has the potential to improve PD-specific symptoms and balance (13).

Did I convince you with those examples? There are even more, but then I am afraid I will lose your attention and making you bored. I hope in this letter I clarify you the reason why human kind has been dancing for centuries. Our ancestors treated it as an important element of their everyday life, not even knowing about its scientific benefits. They were aware of the uniqueness of this activity, and so should we! Nowadays, with modern technologies we are able to prove beneficial effects of the dance not only with psychological and subjective methods, but also diving deeply into brain connections and areas!

So next time you hear the music, don't be shy to dance. Don't limit yourself to just tapping your feet or slightly moving your head. Dance! Don't be afraid that you could look 'silly'. Putting aside all those scientifically proven long-term benefits, primarily we engage in dance for the purpose of intrinsic reward (8). Therefore, this process should be naturally pleasant for us when we set aside shame and inner inhibitions!

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Exploring the labyrinth of dementia:
an historical perspective

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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.

"I have lost myself…"
Auguste Deter to Alois Alzheimer.

- *What is your name?*
- *Auguste.*
- *Family name?*
- *Auguste.*
- *What is your husband's name?*
- *(She hesitates, battling with the depths of her memory) I believe… Auguste.*

This fragment of a long discussion between Alois Alzheimer and Auguste Deter is an example of what dementia can be seen as: being out of one's mind. This article embarks on a journey to unravel the complex concept of dementia, tracing its historical roots while navigating the contemporary landscape of this scientific inquiry.

Our journey begins with the realization that the concept of dementia is far from being self-evident. When the word is used, it gives the illusion of having a meaning in itself. But in general, the word dementia is used in a complete sentence or as a complement to other words. Indeed, we can find name of diseases like 'frontotemporal dementia', 'vascular dementia', or it gives a complement to other pathologies like 'Alzheimer's disease with dementia', 'Parkinson's disease with dementia'. Grasping the concept of dementia is delicate as it requires an interdisciplinary exploration that goes back to the historical roots of neurology.

Hence, we need to remember that medicine did not discover dementia, humans have always seen its effects. Since ancient Egypt, the pioneers of medicine in ancient Greece and Rome: humankind is full of stories depicted persons we cannot recognise anymore. People lost in the world they once knew, seeing their loved ones as strangers. Faced with this helplessness, these poignant situations, situations that interrogate humanity itself… humans ask questions. Or to be more precise, humans try to find answers.

During Antiquity, the first physicians correlated this state of the mind with the brain's functioning. Damage to this organ can cause this apparent 'confusion' in persons.

The first tentative answers came at the same time as psychiatry and later neurology blossomed. In France, it started with Philippe Pinel (1745-1826) who coined the term dementia (but already used in common language since the 14th century) and Jean-Étienne Esquirol (1772-1840). For these alienists a demented person is considered as aliénée, thus the person needs medical assistance. Dementia also starts to be seen mainly as a memory loss. Finally, the concept of senile dementia arises (no longer used in neurology today), meaning normal ageing can be the principal cause of dementia. Dementia is a way of getting through the ageing process.

In Germany, pioneers of neurology are also tackling this question. Carl Wernicke (1848-1905) and Emil Kraepelin (1856-1926) gave detailed description of demented patients and continued the work done by Pinel and Esquirol. Notably, they showed that an anatomical cause of dementia is arteriosclerotic brain atrophy, meaning arteries clogged in the brain leading to brain atrophy. Nonetheless, it is in the group of Kraepelin that Alois Alzheimer (1864-1915) gave an astonishing yet seminal description of a patient from 1901 to 1906. Her name: Auguste Deter (1850-1906). In the famous compendium of psychiatry wrote by Kraepelin in 1910 we can read "…this disease described by Alzheimer." The Alzheimer's disease was born. Our journey is marked by a breakthrough in the understanding of dementia made by Alois Alzheimer. First, Alzheimer was facing a demented woman aged of 51 years old. Since, the concept of pre-senile dementia was invented (Kraepelin put the threshold at the age of 65 years old, above which it is considered as senile dementia). Second, the post-mortem analysis of Auguste's brain by Alzheimer revealed neurofibrillary entanglements and plaques (named after senile plaques).

These discoveries were made in the historical context which the 19th century is dying (but still in everyone's mind) and the 20th century is about to dawn. Inserted in the old dogma that senile dementia cannot be separated from normal ageing or normal senility. By these discoveries of anatomical correlates, dementia is, at that moment, an illness. The 20th century will then become the one of 'biomarkers.' Explaining dementia is still impossible but in every demented patient we will search anatomical and biological correlates to categorize and try to find causes to dementia.

During the 20th and 21st centuries important discoveries were and are still made. Neuroscience found out that neurofibrillary tangles are in fact aggregates of Tau protein and the senile plaques are Aβ aggregates. Later in the 20th century another disciple of Kraepelin, Friedrich Heinrich Lewy (1885-1950) discovered another type of aggregates the well-known Lewy bodies, in fact aggregates of α-synuclein. Also correlated with dementia.

The more scientists are studying Alzheimer's disease, Parkinson's disease, for example, the less dementia is studied. The paradox is the following: after all the efforts dispensed to understand dementia, science has evacuated the problem it claims to address. Dementia became again an elusive concept.

But the answer was already there… Right in front of us all along. Auguste was already saying it to Alois Alzheimer: "I have lost myself…"

Knowing if Auguste was indeed suffering of Alzheimer's disease is still in debate but what we surely know, she suffered from dementia. Dementia is not just about memory loss, Aβ plaques, Tau tangles, α-synuclein aggregates. It seems that dementia is more holistic. What if dementia is simply what humanity has always seen in people who are out of their minds and out of the world?

Dementia can be described as four major changes leading to a fragmented inner world and to an impossible relation with the external world (physical and social):

1) Cognitive: dementia leads to learning and memory impairments, language dysfunctions, and executive functions problems as well as attention and perceptual-motor functions.

2) Emotional: depression, anhedonia, anxiety are often seen in dementia.

3) Neurobiological: Aβ plaques, Tau tangles, α-synuclein aggregates can be found.

4) Social-interpersonal: social cognition and communication are largely impaired, as are problems recognising people.

The ongoing reframing of the concept of dementia has led to its disappearance in the last version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Dementia is now replaced by the concept of major neurocognitive disorder. Even if the word is about to disappear in psychiatry and neurology, dementia continues to exist. People with dementia have always existed, continue to exist and will continue to do so.

The diagnosis is nowadays based on the following criteria: 1) the presence of a cognitive (memory, language, executive functions, etc.) or behavioral disorder objectivized by an appropriate test, 2) an impact on the individual's autonomy (if autonomy is preserved despite the disorder, it is referred to as mild cognitive impairment), 3) this condition must represent a break with the patient's previous state (unlike mental retardation, for example), 4) this state must not be 'acute' (otherwise it is a confusional syndrome) but 'chronic'.

Perhaps something is missing to account for the particularity of dementia. Dementia is acting more deeply and more mischievously in the personhood directly. It is acting on what makes us human: autonomous integrity of self-consciousness and the self itself, rationality, emotionality, appropriateness of social and interpersonal relations. Dementia is an alteration of personality, which may represent the essence of what dementia is.

Our journey through the concept of dementia revealed that studying the roots of dementia is studying the history of neurology itself. The historical perspective appeared to be useful to understand why dementia is a concept difficult to grasp in the 21st century. This is because the concept of dementia has been rendered invisible by, for example, Alzheimer's or Parkinson's diseases. As well as its complete disappearance from the DSM-V. Dementia is the combination of alterations in the cognitive, emotional, neurobiological, and social-interpersonal spheres. But what makes dementia more striking is that dementia alters identity itself.

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Behavioral tuners

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[1]Glia-neuron interactions team, Neurocentre Magendie, University of Bordeaux.

This interview was extracted from the website www.neuronhub.org founded by one of the members of the Editorial Board of BrainStorm (Juan Garcia-Ruiz).

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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The Greek word enteron means gut. You know that the gut is that part of the digestive system located between the stomach and the anus where part of the absorption of nutrients from the food we eat takes place. In it we harbor an exuberant bacterial flora, as well as other microorganisms that do us more good than harm. Almost a century ago, an Italian man named Vittorio Erspamer found a molecule (specifically a monoamine) in intestinal cells that was capable of causing intestine contractions. As he was a very creative man, he wanted to give his molecule an original name, and so enteramin was born (yes, enteron and amine, enteramin, the amine of the intestine). What if I told you that you already knew about enteramin before reading this paragraph? A few years later, Arda Green, Irvine Page and Maurice Rapport discovered a molecule in blood serum capable of modifying vascular tone with a vasoconstrictor effect. Being no less original than our Italian friend, they named this molecule serotonin (you guessed it, serum and tone, serotonin). A few years later they realized that enteramin and serotonin were the same molecule. The latter ended up making its way into our lives and that is how we know this neurotransmitter today. I mentioned that serotonin can induce intestinal contractions and vasoconstriction. But wasn't it the molecule of happiness? I won't answer to this question, but Philippe will. He will also tell us about the importance of monoamines and share with us his vision of the research.

Philippe de Deurwaerdère is a professor at the University of Bordeaux since 2000, after obtaining a thesis in neuropharmacology in 1997. He did his postdoc in Los Angeles, where he lived for a year and a half (but he didn't shoot any film, as he clarified). Then he started working as a professor at the University of Bordeaux. He has been working in several laboratories that have helped him evolve, and currently he holds a position at the Institut de Neurosciences Cognitives et Intégratives d'Aquitaine (INCIA).

Juan Garcia Ruiz: Serotonin is often associated with happiness in everyday life. Given its wide distribution in the central and peripheral nervous system, to what extent is it reductive to attribute this unique role to it?

Philippe de Deurwaerdère: I bought toilet paper with a text that read: "dopamine = love" and "serotonin = happiness". So that's all it is, it's just toilet paper. The role of these molecules cannot be reduced to a function. I will paraphrase two of the greats of serotonin, Jacobs and Azmitia: serotonin participates in all functions without being necessary for any of them. It is a neuromodulator. In the periphery, it also modulates organ activity, including the gut (where 80 to 90% of the body's serotonin is found).

JGR: How can one approach the study of complex neuromodulators such as dopamine or serotonin?

PDD: We have to start from a philosophy of scales. For example, in vitro experiments will allow us to understand the interaction of these molecules with receptors or transporters. This will not explain the function. The scope of a neurotransmitter or neuromodulator can only be pondered through the function of the brain. And what is the function of the brain? The production of behaviors. How does one approach the study of a neurotransmitter system as vast as serotonin? We must never lose sight of this notion of behavior, even if a priori, serotonin itself has little to do with its production. But it is capable of modulating it. It gets very complicated. We can modulate behavior with serotonergic molecules, for example with hallucinogens that target 5HT2A receptors. But these are special cases. Back to the question: how do we do it? We should just not forget behavior, the function of the brain, and the wide distribution of neuromodulators. When we look at the organization of the brain, we realize that serotonin can act in one region and have consequences on the activity of serotonergic neurons projecting to another region. The issue needs to be approached systemically.

JGR: What are the trace amine associated-receptors or Taar1, in a nutshell?

PDD: Trace amines are strange molecules that can be of considerable importance when using molecules such as L-DOPA (editor's note: L-DOPA is the gold standard treatment for Parkinson's disease). L-DOPA, a precursor of dopamine, can give rise to other molecules such as tyramine, octopamine, 3-methoxytyramine, 3-methoxytyrosine, 3-O-methyldopa, etc. All these molecules are considered trace amines, and there is a whole family of receptors to which they can bind with high (nanomolar) affinity. Not only trace amines can bind to these receptors. Also molecules like dopamine can do so. So the nomenclature is nice, but one has to be careful with it.

JGR: What does your research consist of?

PDD: This goes back in part to the earlier question about how to approach monoaminergic systems. The fundamental question of my research focuses on understanding the involvement of neuromodulatory systems in the adaptation of organisms. These systems are the key. But it is a strange key. For example, if we suppress the monoaminergic systems in animals, everything seems to be fine. So what they actually do is to allow a better adaptation of the organism to its environment. I use a neurochemical approach, which has the advantage of being quantitative. Even if the amounts of monoamines are completely different from one brain region to another, we can say that these monoamines are there, that they play a role and that they should be studied.

JGR: Why is it so important to study monoamines?

PDD: The study of monoamines is a kind of basic research that allows us to understand the evolution of an organism in its environment. Humans modify this environment. For example, I just saw this new building being constructed on campus. My calculation of space will soon change because of this building. Our modification of the environment has a considerable impact on how we perceive it and how we act. Right now, climate considerations are on the agenda. This issue is almost anxiogenic. So is covid. We have all experienced that post-traumatic stress disorder on a large scale. Facing these situations there are systems that react, usually for the better. We generate certain behaviors, and monoaminergic systems get involved to enhance them, perhaps to the detriment of other behaviors. But when we return more or less to the old normal, it takes us a while to readapt. Or we don't do it at all. Returning to the old environment can even be potentially negative, because the monoaminergic systems have driven an adaptation, so when we return to the initial situation we may find ourselves a bit lost. That's a what we need to make people understand. Monoaminergic systems are also involved in how individuals evolve with age. Finally, these systems are also studied in neuropharmacology to treat depression, anxiety, schizophrenia, and so on. The study of monoamines can make an important contribution to society in this regard.

JGR: What have been the successes of the pharmaceutical industry?

PDD: Many pharmacological treatments have arisen by chance. Random is wise. What the industry does is to try to explain the mechanisms of action by observing how the molecules work in the nervous tissue. This is the case with schizophrenia, depression, anxiety, and so on. We still do not understand neurodegenerative diseases. We are making progress, a considerable effort is being made, but we do not understand them very well. We don't understand epilepsy either, by the way. The success of the pharmaceutical industry is based on the discoveries of researchers, which is what allows the development of more effective molecules. The obvious success of most of these pharmacological agents, be it L-DOPA, antidepressants or antipsychotics, is to limit side effects and improve pharmacokinetics (better and wider distribution in the body). Significant progress has been made in this area. But we need new advances because we are running out of steam.

In the case of Alzheimer's, antibodies are starting to be developed. But I don't know if we have the necessary handsight to evaluate their success. We will have to wait about 5-10 years to see if all this is functional. The Parkinson's case was different. We had an incredible stroke of luck. Before L-DOPA we knew that atropine could correct Parkinson's, albeit with significant side effects. But for the moment we cannot correct Alzheimer's disease. We don't understand it. Probably what we need is to address its causes.

JGR: What do you think about basic research (as opposed to applied research)? Is it legitimate to study protein X as an end, or should it be implicated in the etiology of cancer?

PDD: Applied research is what we call innovation. Unfortunately in France we have a ministry called the Ministry of Research and Innovation, and that says a lot about the mentality of our government. But it is not the only thing. Our research has a scope of about 3 centimeters forth instead of looking ahead to the next 20 or 50 years, which is what basic or fundamental research does. People don't understand what fundamental research is, because the more we individualize, the more we look at the short term. I think the need for society is to look very far ahead to reposition humanity and biology in general into a global understanding. I'll tell you an example. I have done a lot of work with L-DOPA. Since 1960, L-DOPA has been administered because it is thought to increase dopamine in the striatum. Well, that may not be the case. Millions and millions of euros may have been spent to understand the impact of L-DOPA on striatal dopamine and striatal mechanisms. It may not work that way, maybe everything is bogus. That is innovation. You can develop something within a defined theoretical framework. The problem is that this theoretical framework may be wrong. Fundamental research is all about this. It systematically studies the theoretical framework.

JGR: Recently, members of the European Parliament have spoken out against animal experimentation and have called for a transition to non-animal research. What is your opinion on this?

PDD: I think this issue is beyond the scientific opinion. It is both passionate and political. If we talk about the scientific aspect, I go back to the beginning of the interview: how do we study how the brain works? And there you have my answer. With behavior. A brain outside the skull has no function. You can study the gut in a Petri dish: you add histamine and it contracts. You can study the heart outside the body: add noradrenaline and it pumps. You can study muscle, adding noradrenaline or acetylcholine and seeing what happens. But if you take a brain out of the skull, you have no idea of what's going on. An animal reacts according to its environment, and I'm not just talking about humans. Take the example of dolphins stranded on the shore. What's going on here? We're not going to find an answer by just looking at one of its cells. The debate is not scientific, and I think the politicians are not explaining it well. They should explain that you can't find an Alzheimer's drug by looking at cells. Still, we can consider the complete opposite opinion: a total rejection of life alteration.

Why not? But then we can't ask for wonderful research. It is curious because when we talk about animal research we are talking about all animals. Even the snail. But at the moment there is no problem if we crush a snail.

JGR: How do you see the future of the Academy in the short term?

PDD: There are disparities in Europe in terms of how it works. For example, take the Latin countries: Spain, Italy, France. These countries had a rather republican system, with lifetime positions. This system is beginning to disappear in France, and probably also in Spain and Italy. Research and researchers are beginning to turn to Europe, which offers large calls for projects. This was already very popular in Germany, the United Kingdom, Sweden, the Netherlands, etc. Gradually, these countries (Spain, France and Italy) are beginning to rethink their organization in terms of civil servants. The request from Europe for some countries, including France, is to reduce their expenses in general, and this includes the number of civil servants. So I see the future of the Academy drifting towards an Anglo-Saxon system. The government that was funding the universities will eventually disappear, the universities will become autonomous. This is how it is going to be. In a few years, the price of tuition will skyrocket. This is something I regret, but I see Europe as a steamroller. If you don't fit into the system, it means you're on the margins, with greater difficulty to get a contract. Meanwhile universities are specializing and developing sectors with people that review projects and make them a bit sexier. The system is drifting into something I don't like.

JGR: What have you learned during your years of research?

PDD: I have learned that at the beginning you don't know your question. Your question arises from multiple sources, from many readings. In basic research, the researcher has to find what he is looking for. This has nothing to do with innovation. In general, it is a question that is a bit impalpable. If we go back to the beginning of the interview: how do we approach the study of a certain topic? How do we position ourselves? There are different scales. There are those who take the cell perspective, others the in vitro systems, others rather the in vivo systems and the integration, and others absolutely need to study behavior.

JGR: Do you remember any good advice you were given?

PDD: Yes. It was after my postdoc, and it was given to me by the director of the lab where I did it, who was also a neurochemist. I started to feel neurochemistry was somehow disappearing. It seemed to me that the neurochemistry I was using then was getting a little bit outdated. But my director told me: don't give it up, it will come back. I learned that there were cycles. I don't like cycles. But this means that we are driven by trends and fashions. For example, there are labs that are diving into optogenetics without really knowing what that entails.

JGR: Do you have a book to recommend?

PDD: Awakenings, by Oliver Sacks.

JGR: Do you have a message for readers?

PDD: Neuroscience research continues, for better or worse. I think basic research is still the driving force. Applied research should not be the model, because too much money is spent and it is very time-limited. Basic research is more difficult to tackle, but it has a greater impact.

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Neuromeme

Simon Lecomte, 3rd year PhD student at the IINS

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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 now pursuing a PhD where he is focuses on the role of lactate in basal synaptic transmission, which allows him to combine his research interests in biochemistry, electrophysiology and neurometabolics. Although he speaks near-perfect French, Juan comes from Huelva, Spain. He is also the co-founder of neuronhub (www.neuronhub.org).

Simon Lecomte

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

Ludovica Congiu

Ludovica is an Italian researcher hailing from the beautiful island of Sardinia. After obtaining a master's degree in Neuropsychobiology at the University of Cagliari, she pursued a Ph.D. in neuroscience at the Universitätsklinikum Hamburg-Eppendorf (UKE) in Hamburg. The project focused on characterizing the role of the cell adhesion molecule L1 in affecting mitochondrial activity and metabolism. Currently, she works as an Assistant Ingénieur at the IMN, where she is investigating the role of P2X4 receptors in ALS and anxiety disorders.

Khadija Inam

Khadija is a Clinical Research Associate in the General and University Psychiatry (PGU) Unit of Centre Hospitalier Charles Perrens. With a Bachelor's degree in Applied Biosciences from the National University of Sciences and Technology, Pakistan, and a Master's degree in Neurosciences from the University of Bordeaux, France, she has seamlessly transitioned from the vibrant academic corridors to the cutting-edge realm of clinical trials. Her expertise is mainly focused on the complex spectrum of neuropsychiatric disorders.

Sara Carracedo

Sara is a PhD student at the Neurodegénératives Diseases Institute (IMN). She comes from Pontevedra, Spain and holds a Veterinary Bachelor's degree from the University of Santiago de Compostela and the NeuroBIM Master's in Neurosciences from the University of Bordeaux. Her PhD is focused on understanding the microglial and neuronal role of P2X4 receptor in ALS pathogenesis in which she is interested in neuroimmune interactions, microglial functions, and P2X4 trafficking.

Toshiko Sekijima

Toshiko, originally from New Zealand, is currently pursuing her Master's in Agro-biomedical Science with the University of Tsukuba, Japan. Driven by her interest in the gut-brain axis, she is conducting an internship in NutriNeuro, focusing on the evolution of metabolic and neuropsychiatric symptoms in bariatric patients. With a passion for scientific illustration, she is stoked to be the latest addition to the BrainStorm team!

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