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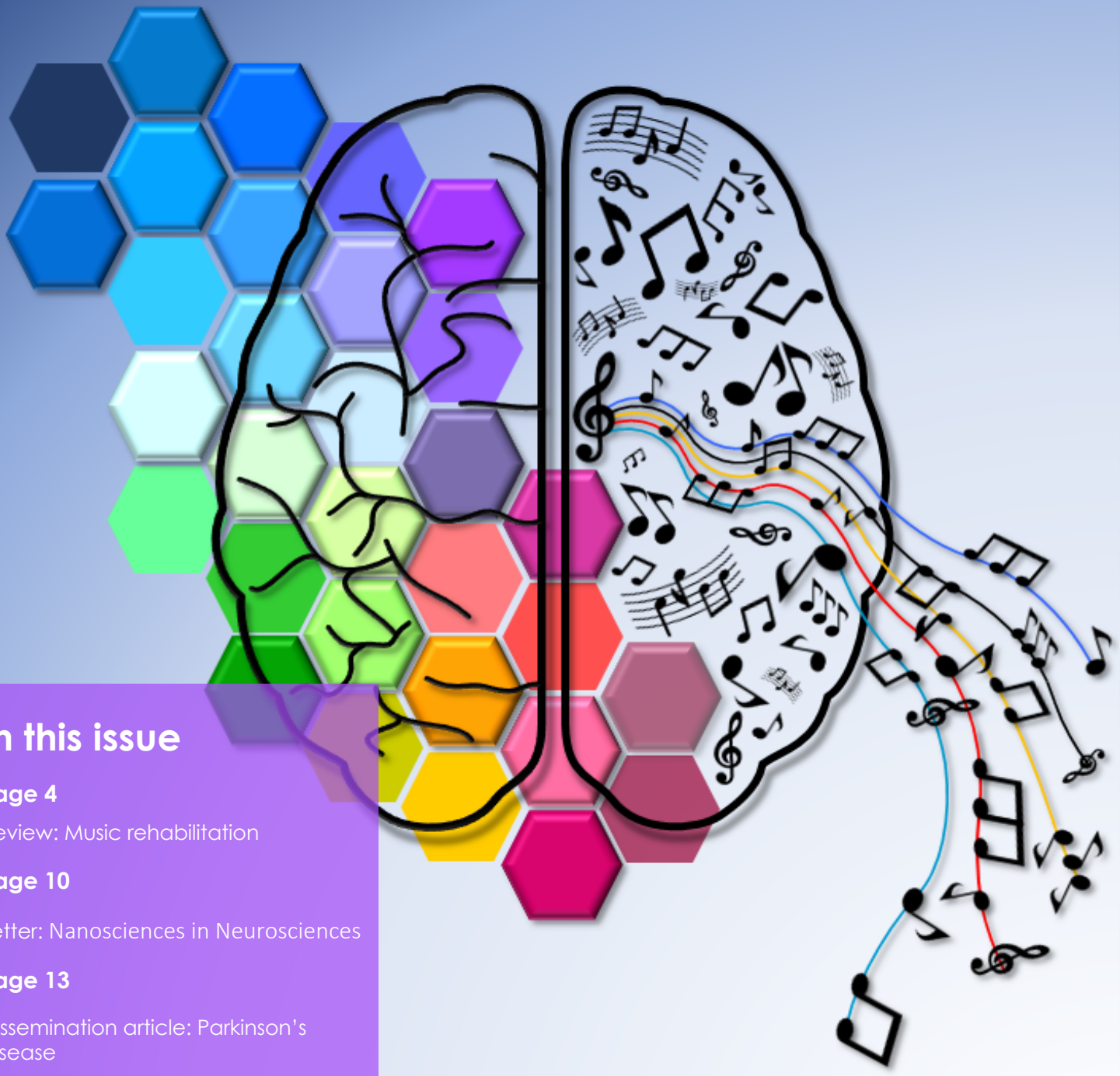

In this issue

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BRAINSTORM STUDENT JOURNAL

REVIEW

Music rehabilitation: a focus on post strokes treatment

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Abstract

Strokes are becoming more and more common, leading to important disabilities. To provide adapted care to those patients, rehabilitation must be thought to improve their well-being. While traditional therapies show great results, they also have their weaknesses. We aim to look at music therapy to see if this is an interesting additional or enough treatment by itself to increase positive results, considering motor abilities, cognitive functioning, mood and pain management. We include a discussion on these effects.

Keywords

cognitive rehabilitation, music, strokes and therapy.

Abbreviations

HIT: high-intensity therapies

MIT: melodic intonation therapy

RTT: repetitive-task training

RAS: rhythmic auditory stimulation

Introduction

Music has been part of our culture for thousands of years. Conveying stories and emotions, translating human creativity, what if it could have even greater powers?

It has been proved that music therapy can be an effective tool for several kinds of disorders. These interventions use music and its components (such as sounds, rhythm, singing) to maintain or improve cognitive functioning or motor abilities that have been impaired, mobilizing those capacities that need training.

Strokes have become a major public health problem in the last decades, various possible outcomes seen after a stroke.

Survivors can experience cognitive deficits, language and speech impairments, motor dysfunctions, or sensory and emotional processing deficiencies depending on the incident localization.

This continuum of cases implies the need of efficient and personalized rehabilitation when there are such persistent symptoms. With over fifteen million new cases every year in the world (1), and an estimate of seven to eight million deaths in 2030 (2), looking at varieties of interventions to reduce post-stroke disabilities could help properly take care of those patients. This consideration leads us to take a look at the benefits of music therapy for strokes.

We can observe two types of strokes. Those incidents can happen for two reasons, respectively: because a blood vessel is blocked by a blood clot, the most frequent case which leads to an ischemic stroke, or because of a blood vessel rupture, leading to bleeding inside the brain, which is a hemorrhagic stroke. Both events, by their very nature, often lead to serious complications as we described before.

Nowadays, high-intensity therapies (3) (HIT) and repetitive-task training (4) (5) (RTT) can be used to improve motor and gait aspects. After establishing the goal, the objective is for HIT to concentrate the patient's effort in short but intense periods of time, and for RTT to repeat a segment of exercise pursuing an increase of the member mobility or general balance and health. We are even beginning to find leads for predictors of response to those techniques (6). However, mobilization of limbs can be painful and tedious.

For cognitive rehabilitation, the effects can be a bit insufficient (7) and scattered. Some remediation can be promising for ones, limited to others. As an example, unilateral neglects seem to improve with strategies implemented in therapy (8) but it overall lacks consistency among all studies (9). Some specific interventions show great results while assessed by the task, such as reaction training for attention deficits (10); but are hardly convertible to everyday difficulties.

Music therapy doesn’t present itself in this context as something willing to replace already existing rehabilitations, but more as a complementary treatment. Our review aims to explore its positive aspects and benefits, and to highlight the kind of deficits responding well to this intervention.

Methods

Articles cited in this review have been found using Google Scholar, PubMed and Cochrane Library.

The following keywords have been used: strokes, strokes epidemiology, music rehabilitation, music therapy, neurologic music therapy, strokes, post-strokes, strokes music rehabilitation, music cognitive functions, music oscillatory activity, music gait, music aphasia.

Results

Motor abilities

Rhythmic auditory stimulation (RAS) aims to use auditory cue, rhythmic sounds in order to help patients with their motor abilities. By providing rhythms they can rely on to move, place their steps or movements… it cues them to give the expected

response. Modulating the tempo of a song during these interventions can help improve the gait (11). Those results show improvement on both symmetry and cadence, but also balance and posture (12).

Promising results have also been found for hemiparesis. RAS can improve the balance and gait of that affected side (13) (14), in a more significant and efficient way than usual gait training. Hemispatial neglect is also a condition that seems to respond well to music therapy, as patients show less collisions in their wheelchairs on their affected side after playing tone bars in spatial organization adjusted to the neglect (15), forcing them to work on that side and engaging attention in an efficient way.

In a more general way, playing an instrument can be an effective training for both gross (16) and fine (17) motor skills for stroke survivors. Indeed, it can improve dexterity, even if longer-term benefits are still studied. However, interesting case studies have shown that playing instruments asking dexterity such as piano allows improvement in upper members functioning (18). But those promising results are not only seen for motor rehabilitation.

Cognitive functioning

Music therapies help with brain plasticity, essential to work on rehabilitation. Because it mobilizes emotional processing, language, and memory (i.e. temporoparietal networks), listening to vocal music then helps engage verbal memory, even more than instrumental music or audiobooks (19). Those results also support evidence for music therapy enhancing language recovery, those results being even more significant in aphasic patients.

While suffering from language disabilities, they often keep their ability to sing.

Already during the 1970s, melodic intonation therapy (MIT) was investigated for those cases and has shown that it helps improve word production in non-fluent aphasia (20) (21).

Research has shown that using a melodic way of speaking, basically moving gradually from singing to speaking while following the prosody of speech (intonation, rhythm, the “music of speaking”) and rhythmic tapping with the left hand engage fronto–temporal regions in the right hemisphere. Engaging those regions is particularly interesting for patients with serious left hemisphere lesions (where language is mostly located) who suffer from nonfluent aphasia, allowing them to work on their language abilities and facilitate the rehabilitation (22).

Not only working directly on these abilities, music also helps with feelings and sensations.

Mood and pain experience

Post stroke depression is often observed (23) in patients. In addition, rehabilitation can be tedious and painful. Music therapy can help manage pain and anxiety for surgery (24). Those results have been broadened to stroke survivors, with results for better care of anxiety (25) and depression (26). Additionally, even when managing pain is not successful, quality of life is better rated by stroke patients treated with music therapy (27). Music therapy appears as an interesting tool to include with or during other interventions when heavy and painful.

Combining usual treatment with music have shown evidence for more positive responses and engagement while performing upper extremity exercises (28). Music was played and karaoke was used, leading to an overall more enjoyable moment perceived by the patients. Even if those results are significant and very promising, it is also important to keep in mind that those interventions aren’t perfect.

Discussion

First, not every result in the literature has been replicated or is stable through a very important period. It would have been interesting to add other evaluations after a very longer period to verify the long-term gains.

Secondly, some results seem to be task specific. A few studies, even with significant results, evaluate the improvement with a neuropsychological task or a clinical assessment. As it doesn't include other assessments, results can’t always be broadened from the task to daily life and the struggles patients can experience.

Going through all of the studies shows us that

outcomes can be diverse. It seems important, while music therapy expands, to identify the successful parameters that allow proper setting for rehabilitation.

Lastly, some variables such as mood and quality of life assessments are subject to subjectivity. Patients' engagement seems essential in those cases to highlight what is “pleasant” to them, and this subjectivity parameter can make results vary.

Conclusion

Overall, we were able to find both very interesting and promising results in favor of the use of music therapy. It seems to help improve motor abilities that have been impaired after the stroke, as well as to help working on cognitive aspects.

It appears as a great addition to already existing therapies. Its ability to modulate and manage pain and anxiety can help increase the mood and the engagement of patients while working with other treatments, making it more pleasant. It also provides new support as a rehabilitation tool by itself : offering new ways of working, adding another possible choice to make when thinking about rehabilitation. While strokes lead to heterogeneous profiles, having more and more options to personalize rehabilitation is precious.

Even if it seems important to still study long term benefits and replicate some experimental procedures, such a potentially enjoyable implementation is promising if we keep in mind that subjectivity can come into play and that outcomes must be correctly assessed to show proper results. Including such things as music into medical care and therapy seems beneficial, and maybe it could even be interesting to take a look at its effects on health professionals providing those kinds of therapies.

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LETTER

Nanoscience in neuroscience

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Nanotechnology has revolutionized the field of biomedical sciences, including neuroscience. Nanostructured materials play a significant role in understanding brain functions and neuronal circuits. Furthermore, they have recently paved the way for new research tools, diagnostics, and therapeutic options for central nervous system disorders (1). Nonetheless, I feel that neuroscientists in general, often coming from pure biological studies, do not have the background to fully grasp what a nanomaterial is and its implications. In this short letter, I would like to briefly introduce the principles governing nanomaterials and mention some of their current applications in neuroscience research.

In December 1959, Richard Feynman, Nobel prize winner and one of the most renowned physicists of his time, gave a celebrated lecture: "There's Plenty of Room at the Bottom", forecasting the exciting properties materials would present when approaching the nanometric scale. This lecture is now considered by many the inauguration of a new scientific field: Nanoscience (2). Classical definitions of nanomaterials often include objects that have at least one dimension under 100 nm. I would go a bit further. Yes, size matters: smaller objects have easier access to microenvironments. This is not the most interesting though. Two key aspects become especially relevant when moving into the nanometric scale: surface/volume ratios and/or quantum effects. The ratio between surface and volume is far from being a trivial property. As materials become smaller, a larger proportion of their atoms or molecules are located at the surface, impacting their reactivity and properties. This increased surface area enables enhanced interactions with other substances, making nanomaterials ideal for applications in catalysis, sensing, and drug delivery. This has a second key consequence: nanomaterials don't behave in the classical way their macromolecular counterparts do. As the size of objects gets closer to the atomic scale, the quantum effects that govern the particle world become more and more relevant. Let us take the example of quantum dots (QDs). These are semiconductor spheres with diameters between a few

and few tens of nanometers. Because of their small size, a phenomenon called quantum confinement emerges, leading to discrete energy levels (like atoms and molecules). They display fluorescence the same way molecules would do, but with a photostability and brightness unthinkable using single classic organic molecules.

In the last few years, the influence of this new scientific field in neuroscience research has been immense and cannot be fully appreciated, nor covered, in this letter. Among their applications, nanomaterials can be used for tissue regeneration through nanofibers, for cellular activity recording through nanowires, for drug delivery and imaging with metallic nanoparticles, and even for templating the growth of axons with carbon nanotubes (5).

In Bordeaux, there have been quite a few interesting studies that used nanoparticles – for instance for Single Particle Tracking (SPT). The SPT of nanometric objects represents undoubtedly one of the major breakthroughs in neuroscience imaging in the last decade. The fact that researchers can now super-localize a single emitter and track it for longer periods has given us unprecedented information about how single objects move in our brains. As relevant examples we can cite the use of QDs to tag and understand the dynamic of receptors diffusing in the membranes (Figure 1b) (3) or the track of carbon nanotubes to understand the diffusion of large objects in the extracellular space in health and disease (4). Last but not least, there is a wide range of nanomaterials that have great potential as nanocarriers, either for specific and stable drug delivery or by their direct action (6). For example, injected acidic nanoparticles can help to restore lysosomal function, alleviating the symptoms in in vivo models of Parkinson's disease (7). Nonetheless, this is still a relatively new field. As we continue to explore and harness the capabilities of nanomaterials, it is essential to address safety concerns, ensure ethical use, and collaborate across interdisciplinary boundaries to unlock the full potential of these tiny, yet powerful tools in the field of neuroscience.

To conclude, two ideas to take home. First, things behave differently when they become smaller. Secondly, nanoscience is already everywhere, and its presence is going to continue to expand. Nonetheless, we still need to learn a lot, including their potential risks, which are likely to be important, so keep them away from your mouth and lungs.

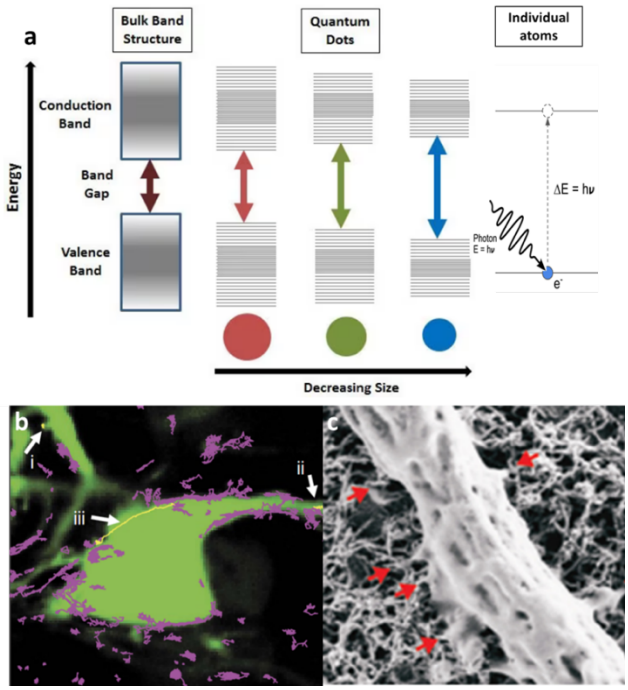

Figure 1. a. Diagram showing the energy levels changes of a semiconductor as it becomes smaller. As QDs become smaller, so does their excitation/emission wavelength. **b.** Trajectories of membrane receptors reconstructed by SPT tracking using QDs. **c.** Axon grows using carbon nanotubes as the template. Red arrows show intimate contacts of the fiber with the carbon nanotubes carpet.

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DISSEMINATION ARTICLE

Beyond tremors: a brief exploration of Parkinson's disease

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Revised by Dr. Abdelhamid Benazzouz

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 would never say that I'm grateful for Parkinson's in any way, but it has allowed me to explore areas of my life that I never would have explored otherwise." (Michael J. Fox)

Known for his memorable role as Marty McFly in 'Back to the Future,' Michael J. Fox has also garnered attention for giving his name to one of the most important foundations funding research on Parkinson's disease (PD), indeed called Michael J. Fox Foundation. The actor has unfortunately been living with the disease for years, but he has always sought to be a spokesperson for positive messages and support for those, like him, facing this daily battle.

But let us talk a bit more in detail about PD. First described by James Parkinson in his 1817 publication, "An Essay on the Shaking Palsy", it is a complex neurodegenerative disorder affecting 1-2 per 1000 of the population at any time, with prevalence increasing with age (1). Approximately 1% of the population above 60 years of age is affected (1, 2) with both environmental and genetic factors contributing to its pathophysiology. Currently, most of cases have unknown etiology, while only 5%-10% of cases represent the genetic forms of the disease (1, 2). Cardinal symptoms of PD include tremor at rest, muscle rigidity, and bradykinesia (or slowness of movement). Diagnosis relies only on clinical findings, supported by adequate testing.

Understanding Parkinson's disease

At its core, PD is characterized by the gradual neuron-degeneration in a brain area called substantia nigra (SN) of a specific group of neuronal cells known as "dopaminergic neurons"(2). They are in charge of the release of dopamine (DA), a neurotransmitter responsible of modulating the activity of other neural groups, like those controlling movement. Disease evolution is associated with a progressive loss of these dopaminergic neurons in the SN and the presence of Lewy Bodies in some of the survival dopaminergic neurons. Lewy bodies notably contain protein aggregates of α-synuclein, probably the most known hallmark of PD. Beyond this, PD may present widespread pathology in other brain regions, involving non-dopaminergic neurons as well. Clinical diagnosis is primarily based on motor features, such as a slowly progressive asymmetric resting tremor, cogwheel rigidity, and bradykinesia (2). Based on these clinical features, PD is categorized into two main subtypes: tremor dominant PD and postural

instability and gait difficulty (PIGD). The first form is characterized by presence of tremor in addition to akinesia and rigidity, while PIGD presents akinesia and rigidity without tremor (3). Non-motor features, including anosmia, constipation, depression, and REM sleep behavior disorder, may develop years before motor deficits (4). Additionally, urinary urgency, sexual dysfunction, hypotension, anxiety, depression, color vision impairments, and dysexecutive syndrome have also been described to antedate the onset of motor symptoms in PD. Non-motor symptoms are likely related to the neurodegeneration of other structures, including the peripheral autonomic nervous system and they tend to increase in severity with disease duration. During the course of the disease, they can cause an important burden and strongly affecting the quality of life of the patient. Particularly, cognitive decline and hallucinations are a common cause of hospitalization and institutionalization in the advanced state of the disease (4, 5).

Treatment Approaches

There are currently no curative treatments, but only therapeutic approaches aimed at improving the quality of life for the patients. Among the various options for PD treatment, it is worth mentioning levodopa. This molecule remains the drug of choice for treating motor symptoms of PD (6, 7). It is a precursor of dopamine, and once introduced into the brain, it is converted into DA, compensating for the deficiency of neurotransmitter at different brain structures. However, long-term therapy leads to levodopa-induced dyskinesia (LID). LID refers to involuntary movement other than tremor and might be due to an increased activity of the direct striatal pathway and impairments of the activity of glutamatergic and metabotropic receptors (8). Furthermore, it can also be a consequence of an abnormal pulsatile stimulation of dopamine receptors (8). In order to delay the onset of dyskinesias, patients are treated with dopamine receptor agonists at the start of the disease, and once they lose their efficacy, levodopa treatment is started.

An alternative to levodopa is the deep brain stimulation (DBS) of the subthalamic nucleus (STN), a very small brain structure important in the control of movements. This is a surgical therapy used to treat certain aspects of PD. It consists in inserting electrodes into a targeted area of the brain, using magnetic resonance imaging (MRI) and, at times, during surgery, recordings of brain cell activity. The electrodes are then connected to an implantable impulse generator battery (called an IPG), which is similar to a heart pacemaker and approximately the size of a stopwatch (7). Based on basic neuroscience and the understanding of the pathophysiology of PD, STN DBS has been first developed in a monkey model of PD in Bordeaux (Benazzouz et al., 1993) before its transfer to parkinsonian patients in Grenoble (Limousin et al., 1995). This neurosurgical approach is now considered as a treatment of choice for idiopathic PD, which opened the way to its application to other neurological and psychiatric disorders. Adaptive DBS (aDBS), where stimulation is applied according to the level of pathological activity, is also experienced in a number of centers (9). In addition to these medical and surgical treatments, it has been shown that physical activities such as sport, intensive walking and physiotherapy can help delay the progression of the disease. Other strategies, such as the practice of mindfulness meditation and yoga, have also been shown to improve patients' quality of life.

Conclusions

PD shows a complex interplay of genetic and environmental factors. Although we usually think about PD as having purely physical symptoms, it actually comes with important psychological load like sleep problems, anxiety or apathy. This calls for a more comprehensive study that encompasses not only the physical aspects but also the emotional and psychological dimensions of the patient's journey. As research continues to advance, the hope is that innovative treatments and supportive measures will progressively enhance the lives of those affected by this complex neurodegenerative disorder.

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INTERVIEW

The necessity of a big picture science

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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 hippie movement that seeked to alter consciousness with drugs such as LSD and marijuana coincided in time with the most prodigious research on highness. The discovery of the receptors involved in cannabis mechanism of action not only helped us understanding what happens when people get high, but also led to the discovery of a crucial nervous modulation system involved in multiple physiological functions like learning, memory, sleep and food intake. The endocannabinoid system involves receptors such as CB1 (remember this, it will be helpful in a little bit) and little lipids synthetized by our system that are able to bind to those CB1 receptors. These lipids are known as endocannabinoids and are very similar in structure to tetrahydrocannabinol (THC), the psychoactive component of marijuana (Figure 1).

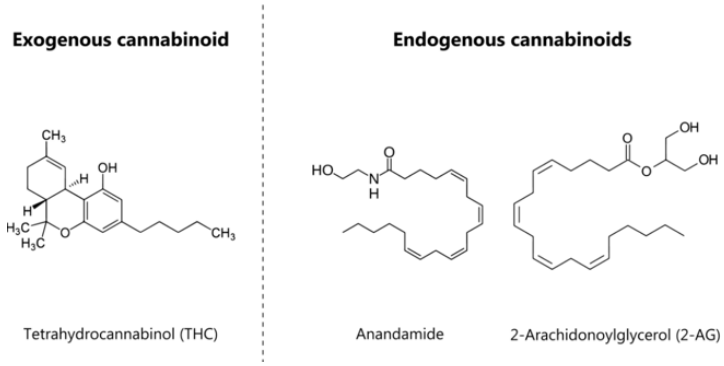

Figure 1. Chemical structures of cannabinoids. Exogenous on the left and endogenous on the right.

Let's now focus on the endogenous cannabinoid system, the physiological one that functions in our system by default with no need of exogenous cannabinoids like THC. How does it work? CB1 receptors are not the only cannabinoid receptors expressed in the brain, but are the most numerous. They are spread across all brain regions, and depending on where they are activated the final output can be different (regulation of food intake, pain, temperature, etc). However, the molecular mechanism of action remains essentially the same. What is that mechanism? CB1 receptors are located at the presynaptic level, in the membrane of a neuron A that communicate with a postsynaptic neuron B by releasing neurotransmitters. When the neurotransmitters are released and bind to the receptors present at the postsynaptic neuron, this one will respond to that by opening or closing different ionic channels, so that its electric potential will change. This will result in subsequent postsynaptic effects: action potential triggering, release of other neurotransmitters, intracellular changes, etc. Among the cellular processes that can take place at the postsynaptic level after neurotransmitter binding there is the release of endocannabinoids, that can go back to the presynaptic neuron. What happens next? When the endocannabinoids bind to presynaptic CB1 receptors they reduce calcium influx by blocking some voltage-gated calcium channels, an essential element for neurotransmitter release. In addition, the binding also leads to an increase in potassium efflux through a channel known as GIRK (G protein-coupled inward rectifier K^+), so the neuron is hyperpolarized and the probability of spontaneous action potential occurrence is reduced. In other words, neuron A sends neurotransmitters to neuron B, and B responds back by sending endocannabinoids and telling the neuron to calm down, to be less excitable and to send less neurotransmitters. This mechanism of retrograde transmission helps the neuron to finely regulate the amount of transmission. It is a way of properly tuning the communication between neurons.

Now you understand the basics of the endocannabinoid system. But there are so many interesting things to know about this exciting field. If you want to become a little expert on one of the most important systems in our brain, you should definitely meet Giovanni Marsicano. Luckily for you, we have interviewed him so you just need to carry on the reading. And do not worry, the molecular part is over!

Juan García Ruiz: Your lab is internationally known for the study of cannabinoid receptors. What are these receptors, in a nutshell?

Giovanni Marsicano: They are regulatory receptors. You could survive without them but they are very important for the fine tuning. I will explain it with an analogy. When you use a microscope you have a coarse-grained wheel that allows you to change the depth at which you position the focus quickly but with low precision, and then you have a finer wheel that allows you to position the focus exactly at the depth layer you want. Cannabinoid receptors are like this fine wheel, and they tune the general functioning of the body.

JGR: When did CB1 receptors appear in evolution?

GM: The first elements of this system that appeared were the endocannabinoids, which are lipids that act as ligands of cannabinoid receptors. Early species showed the ligands I just mentioned but not the receptors. Reptiles are the first species to show something that really looks like a cannabinoid receptor. There is the idea that one of the main functions of cannabinoid system is favoring energy accumulation. Energy accumulation is a feature that allow species to prepare to face an uncertain future in which energy will be needed and maybe the sources will not be available. The specialization of energy accumulation comes with fat. The adipose tissue turns out to be present already in reptiles. Otherwise said, cannabinoid receptors appear in synchrony to adipose tissue and their specific ability to accumulate energy.

JGR: What kind of questions are you trying to answer in your lab?

GM: Our lab has a specific philosophical background. The brain is a complex, redundant and connected machine. This means that by using the typical scientific approach that is specialization, there is a risk of loosing some part of information. If you go too much into details then you do not see the general picture, which is very important in this field. If you take a fruit fly and a human, there are no enormous differences at the smallest levels. The great differences come when you consider the big picture, and that is why it is so important to find a good balance in specialization. The good thing for us is that CB1 is involved in so many things in the brain that we are highly specialized since we study just a few different proteins, but at the same time we go in many different directions, so we keep the "big-picture mindset". For instance, CB1 have different functions in neurons, astrocytes, and microglia. So another way to see it is that we use CB1 to understand the complexity of the brain.

JGR: Did your lab made a discovery that you are particularly proud of?

GM: Yes, the discovery of the mitochondrial CB1 receptor. It was very hard to defend, and it is an example on how science can be the result of serendipity. First, I need to give you a little bit of background. THC, the psychoactive component of marijuana, was discovered in the forties and became very famous in the sixties. For almost 20 years we did not know how THC was working in brain cells. If you look at the publication rate related to this topic, you have a peak in 1964. It was something very cool at that time to put THC on everything and say you were working on *highness*. Some of the publications that came out suggested a mitochondrial effect of THC. Then in 1990 the receptor of THC, which is a GPCR, was discovered. But something weird was going on: GPCRs are not present in mitochondrial membrane and are by definition present at the plasmic membrane. So the results were explained as a non-specific effect of THC: mitochondrial membrane is sensitive to lipids, and cannabinoids are lipids, so if you use a lot of lipids you can alter mitochondrial membrane and therefore mitochondrial functioning. Fine. So the data suggesting that THC affected specifically the mitochondria were discarded.

JGR: But then you proved that CB1 could actually be expressed on mitochondria. How?

GM: I met Pedro Grandes, a neuroanatomist from Achucarro Basque Center for Neuroscience, I asked him: have you ever seen CB1 on mitochondria? And he told me: yes, but everything we see is just background staining. He explained that what people in the field were doing was to normalize the CB1 expression in the plasma membrane to its expression in the mitochondria, considered to be noise because it was believed to be impossible to have this receptor expressed there. Then I sent him some knock out animals (editor's note: animals modified genetically so that CB1 receptor was not expressed) just to see if this background staining he saw in the wild-type animals (editor's note: non-genetically modified animals) was still present. After several months, he came back to me with images that he took with electron microscopy by using immunogold staining on CB1 receptors. I did not even remembered about this. And surprisingly we found out that knock out animals did not show this background, suggesting that the signal we observed at the beginning was not just noise, but actual mitochondrial CB1 receptors! We received a lot of criticism. A paper was written to directly attack our discoveries by saying that everything we saw was background, and then we replied with another methodology paper comparing our methods with theirs, and we concluded that their method was not sensitive enough to detect the receptor, and the difference of the results came from this methodological problem. The way we proceed nowadays is by trying to refute the existence of this mitochondrial CB1 receptor, but so far we have not managed to do that! So this is the discovery I am the most proud of.

JGR: What philosophy do you try to foster in your lab?

GM: One idea I like to promote is the one we talked about before: in neuroscience we have to be specialized, but at the same time open to understand other subfields and try to have a general vision. As for the human aspect, when people come to my lab to work, I always tell them I do not care how many

hours they do, how many holidays they take. I really do not know what they do, when I have to validate something I do it automatically. I want people in my lab to be aware that they do not work for me, but for themselves (with me). If I tell you to do this and that because I like it, but turns out you do not like it, then it will not work! So telling people to do everything for themselves makes them more happy to work. And it is important because our work is crazy. We have very few satisfactions, but it seems to be enough. This small thing you get from time to time, a stupid graph that shows you something worked, makes you happy for months. So you need to be a bit crazy to do science.

JGR: What are the most valuable features that a good scientist should have according to you?

GM: The first one is curiosity for sure. One needs to read a lot, and not only scientific stuff. The second is rigour, self-criticism. I surround myself of science-policemen. For instance I was very lucky to start working with Francis Chaouloff fifteen years ago because he is a real policemen. Whenever I am enthousiastic about something he will make me calm down, check the statistics, the controls, and every kind of detail that we could overlook by mistake. When you follow something you do not see the rest. Cristopher Stevens, a student from the neurocampus was working on this, on the confirmation bias. You see physically only the things that confirm what you think at the beginning. But it is also important to keep the enthousiasm or if you prefer the craziness, and this would be the third feature. There are some jobs that people choose for convenience: when you work in a bank, or when you are a lawyer. Even if you do not like your job, you can do it for convenience and then do nice stuff with your life. But other jobs are actually your life: when you are an actor, or a musician. You do not choose this for convenience. I think being a researcher is more similar to the second type of job, where you need some vocation to overcome all the stressing situations and so on. So to sum up a scientist needs to have curiosity, rigour and enthousiasm.

JGR: Would you give an advice to the readers?

GM: For young people, what I always say is: understand what you like. It takes time to know what one likes. I know it is not their fault, but I sometimes see students that come and say: so now I am in my first year of master, next year I will do the second one and I will do my internship this lab or this other one, then I want to do a PhD here or there, and they have everything figured out from the beginning! All I can tell them is: good luck. I am sure that nothing will go as it was planned. A lot of things happen by chance. What I can suggest them is to try to understand what they like and to be as open-minded as possible, to keep eyes and ears as open as possible, and not to be afraid to ask questions.

JGR: Do you have a final comment you would like to share?

GM: Something I would like to explore more deeply and encourage people to explore as well is evolution. In my lab we always go out to celebrate the birthday of Charles Darwin. This is not only to have fun. In my opinion to understand how things work we should not forget about how they evolved to get to that point. I am not saying that Charles Darwin is like the Holy Bible, but we celebrate its birthday because his character is like a symbol for evolution. Nowadays you hear about Lamarck and you almost laugh. The explanation of natural selection of Darwin has been key for us. But I realized after reading *The Origin of Species* that Darwin was not so in disagreement with Lamarck ideas of transmission of acquired traits. And nowadays we have epigenetics, which is actually not going against Lamarck. The problem with human is that we like to build churches and create dogma even in science. My last comment for the readers is to avoid building churches.

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Neurometeme:

Simon Lecomte, 3rd year PhD student at the IINS

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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—Schizophrenia, Depression, Anxiety, and Bipolar Disorder.

Juan Garcia-Ruiz

With two Bachelor's degree, in Psychology and Biochemistry, and the NeuroBIM Master's degree from the University of Bordeaux, Juan is 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).

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 role of P2X4 receptor in ALS pathogenesis and biomarker in which she is interested in neuroimmune interactions and receptor trafficking.

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 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 getting a master's degree in Neuropsychobiology at the University of Cagliari, she successful pursuit of a Ph.D. in neuroscience at the Universitätsklinikum Hamburg-Eppendorf (Uke), in Hamburg. The project was focused on the characterization of the role of the cell adhesion molecule L1 in affecting mitochondrial activity and metabolism. Currently, she's working as an Assistant Ingénieur at the IMN, where she is investigating the role of P2X4 receptors in ALS and anxiety disorders.

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