Neuroplasticity, for better and for worse

Neuroplasticity is the brain's ability to change its structure and function by interaction with the environment. It takes place at various levels of complexity, from the molecular pathways within neurons to the intricate circuits that connect them.

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Executive summary

Neuroplasticity is the brain’s ability to change its structure and function by interaction with the environment. It takes place at various levels of complexity, from the molecular pathways within neurons to the intricate circuits that connect them. However, sometimes the environment is harsh with the brain, causing developmental disorders of children and neuropsychiatric diseases in adults. In this case, neuroplasticity provides the brain with the possibility of compensating for the impacts on its structure and function. But sometimes this process goes wrong, and symptoms take place as a result of maladaptive plasticity. What predominates, in the end, is the great possibility of taking advantage of the way one brain can change another brain by reciprocal interactions—”transpersonal plasticity”—as is the case in education.

The different levels of neuroplasticity

Many years ago, I read a book that impressed me very much, written by the British biochemist Steven Rose[1]. Rose explored the idea that all natural phenomena and objects have a multiple existence—or at least can be approached from different *heuristic levels*, as he called them. A good example is the ”object” Earth. For an astrophysicist, our planet is no more than a minuscule grain of powder moving together with thousands, millions, billions of similar grains within the almost unthinkable dimensions of the universe. For a geologist, on the other hand, Earth is a gigantic sphere formed by a set of layers one over the other, of different thickness, composition, temperature, and physical state. For a particle physicist, however, Earth is perhaps of astounding simplicity, constituted by no more than 20 elementary particles, and nothing else. Botanists and zoologists are interested only in the Earth surface, that is, in the plants and animals that inhabit it. And anthropologists and sociologists focus on only one of these numerous species: humans. The object of interest of all these scientists, however, in the end is the same—the Earth—studied at the same time under different views or, as Rose called them, different heuristic levels.

Each level requires a specific scientific approach, with particular methodologies, often times exclusive of each one of them. Put simply, it is useless to employ a telescope to analyze the chemical composition of the sea, or a structured questionnaire to study the behavior of quarks.

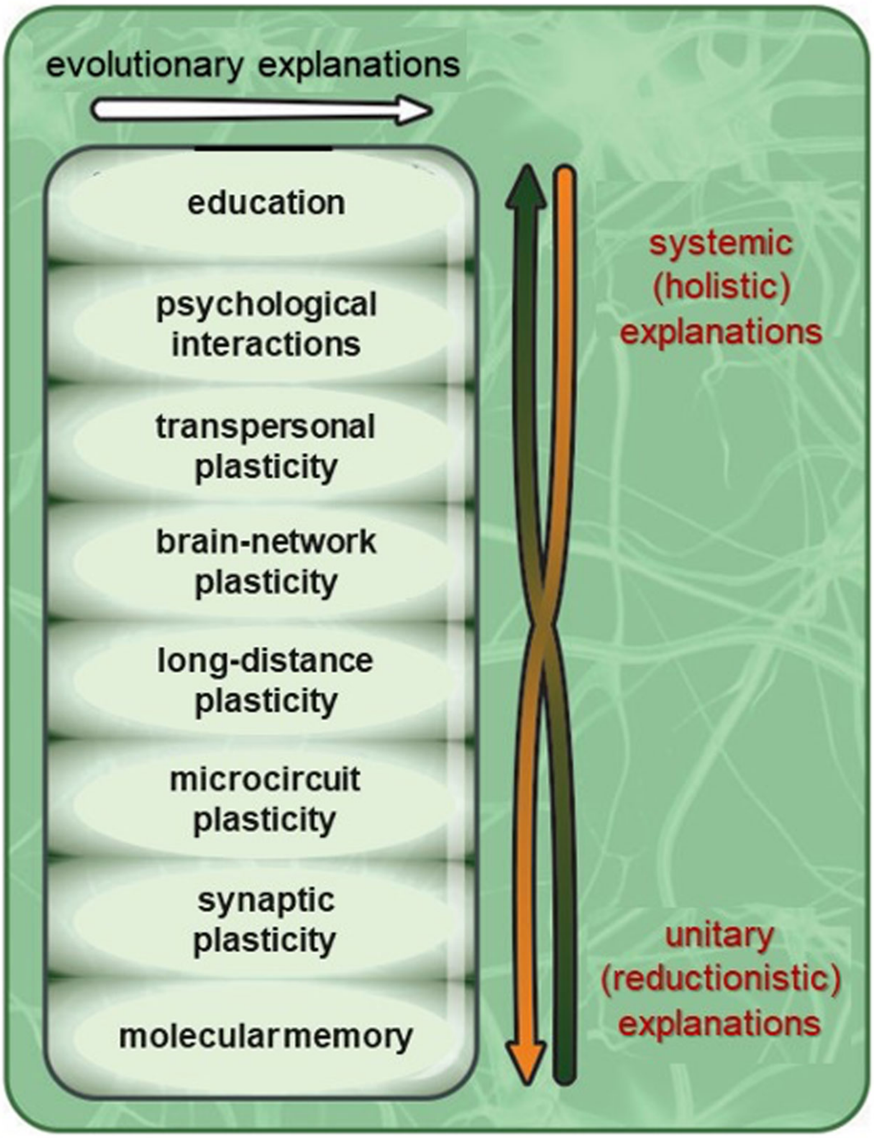

Figure 1. The different heuristic levels of neuroplasticity. Modified from Lent (2019), *The Apprentice Brain*[2](illustration by Julio Xerfan).

The same argument can be employed concerning the brain and its functions. It can be approached from the molecular pathways of neuronal metabolism and of synaptic transmission, objects of study of neurochemists, to the greatly complex multipersonal, behavioural phenomena, which are the objects of psychologists. Rose called attention to the simultaneous existence of these different heuristic levels, and criticized the narrow, one-sided views proposed on the one hand by the so-called reductionists, and on the other hand, with an opposing stance, by those known as holists. For the former, mental phenomena could be entirely explained by reducing them to their molecular and cellular mechanisms. For the latter, mind would be at most an emerging property of the brain, with an existence independent of it. The great challenge, therefore, is to establish bridges between these heuristic levels and extract the most of looking at phenomena from different angles of view. I will here apply this conceptual framework to neuroplasticity.

Neuroplasticity can be defined as the ability of the brain and its functions to undergo transient or permanent changes after being influenced by the environment, external or internal. External influences are provided by nature, society, and other human beings and their brains, while internal influences derive from the workings of the subject's own brain. There are many different levels of neuroplasticity (see Figure 1), but for the sake of simplicity one may consider the following: (1) *molecular/cellular level*, within neurons and glial cells; (2) *synaptic level*, in the junctions that allow communication between neurons and also glial cells; (3) *microcircuit level*, considering chains of interconnected neurons in close proximity; (4) *long distance level*, including the long tracts of fibers within the brain white matter; (5) *systemic level*, involving active and interactive neural networks connecting a whole set of brain areas; (6) *transpersonal level*, which includes interactions between brains/persons (as that of a teacher and a pupil); and (7) *psychosocial level*, considering pairs, groups, or even populations of human beings with some kind of structured social organization. We can say that all these levels of neuroplasticity contribute, at the same time, to provide human beings and their interactive brains with the incalculable exchange, storage, and retrieval of information of which they are capable.

Compensatory plasticity, not the perfect remedy

Whatever the level one considers, one's tendency is to expect a good result from the ability of the brain to change its synapses, circuits, tracts, or networks. Plasticity is, therefore, viewed as an always-beneficial property of the nervous system.

Indeed, there are many examples that this can be so. Learning is one of them. Seen from a reductionistic approach, learning results from the capacity of synapses to retain for some time the information being transferred from a given neuron to another. Under certain conditions, gene expression within connected neurons is modulated and results in the synthesis of molecules that will eventually be transported to the active synapses and contribute to strengthening them for times longer than a short moment. Seen from a more holistic angle, learning activates a great number of synapses forming circuits and networks, and this entire machinery becomes the repository of something we call knowledge. This is the way we learn how to read during school times. Certain areas of the cerebral cortex performing complex visual functions such as the recognition of faces, biologically important for our survival in society, are used to keep the memory and recognize (retrieve) letters, words, sentences, and associate them with the sounds of our language[3]. The beneficial results of neuroplasticity are associated with sensitive periods of life, during which our nervous machinery is more susceptible to be changed by the environment.

Stretching the argument to an extreme point, one would expect that early disorders of brain development could be entirely (or mostly) compensated by neuroplasticity. This was what Roger Sperry—Nobel prize of medicine or physiology 1981—suggested when he came across a young woman who did not have a corpus callosum[4]. This is the largest white matter tract in the human brain (see Figure 2A), accommodating around 200 million fibers that interconnect reciprocally the two cerebral hemispheres. Sperry's own work had discovered the famous interhemispheric disconnection syndrome in patients after surgical transection of the corpus callosum as a treatment for severe epilepsy[5]. Following surgery, these patients were unable, for instance, to point to an object with one hand after trying to recognize it with the opposite hand, with eyes closed. Simply put, the corpus callosum was not there to transfer the information about the object from one hemisphere to the other, so that one hand could not share the information obtained by the other. How come, then, people with callosal agenesis—small or no callosum at all since conception—were able to perform this task perfectly?!

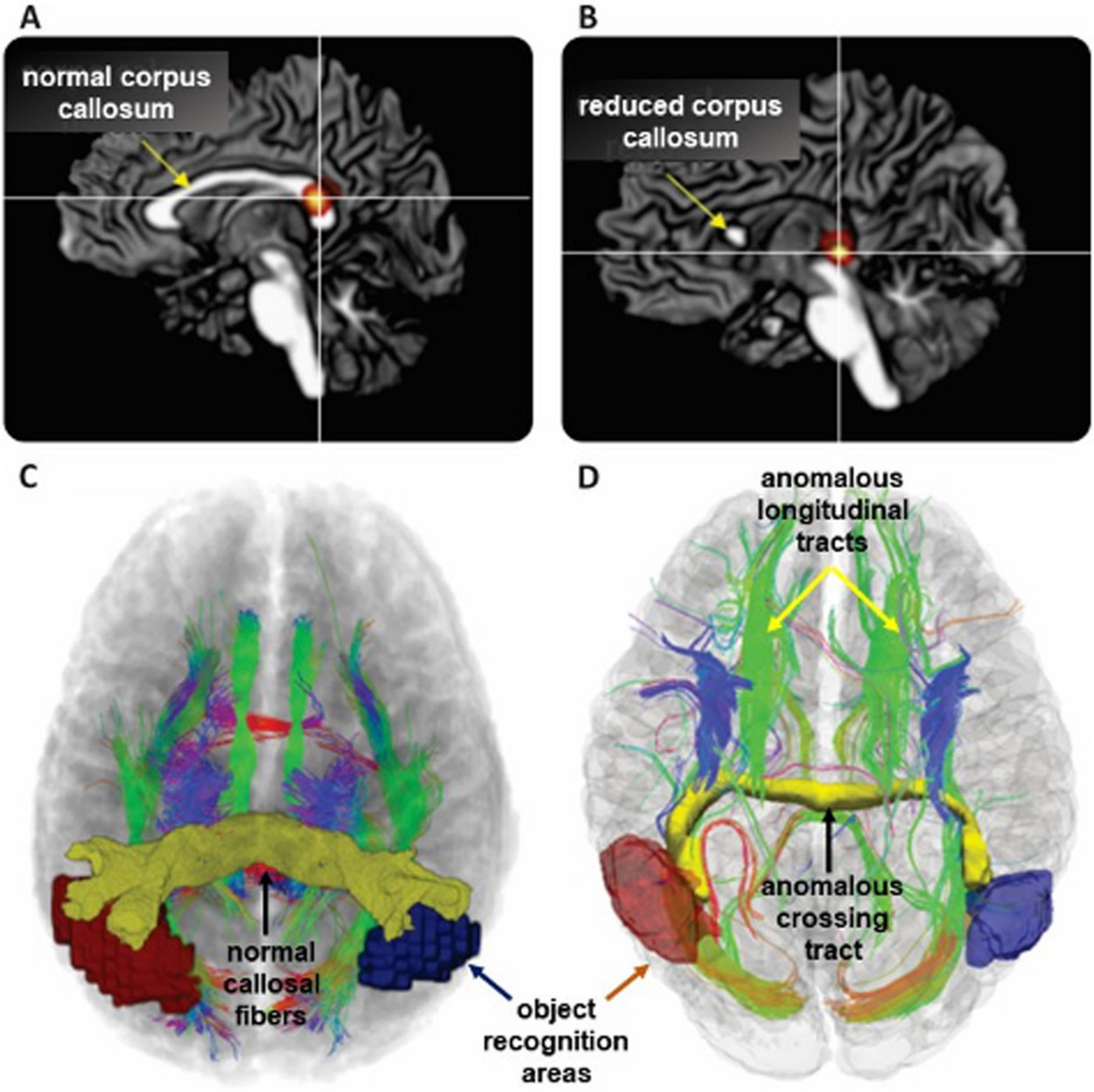

Figure 2. A shows the midplane view of the brain of a typical subject, with a normal corpus callosum in white, pointed by the yellow arrow. B shows a highly reduced callosum shown at a similar angle of view, from a dyscallosal subject. The yellow/red regions in the callosum show the position of the interhemispheric fibers in charge of crossed tactile object recognition. C shows the pattern of circuits of a typical subject, in comparison with D, that illustrates one of the dyscallosal patients. The yellow tracts connect the tactile recognition areas in the cortex (in red and blue). Modified from Lent (2019), *The Apprentice Brain*[6]

My collaborators and I in Rio de Janeiro were curious about this mysterious phenomenon and investigated the possible reasons for this compensatory outcome of neuroplasticity in acallosals. We first did a neuroimaging study of the brain of these patients and confirmed that they had different degrees of callosal dysgenesis[7]: some had it complete, others displayed very small callosal remnants (see Figure 2B), and a third group had a callosum of reduced size. In all cases, we could clearly see the presence of a huge, uncrossed anomalous fiber tract of longitudinal trajectory, and another longitudinal tract which crossed the midline through the callosal remnant of some of these patients. The most interesting finding was the presence of anomalous tracts connecting two homologous brain regions of both hemispheres and crossing the midline through alternative places situated far from the crossing point normally used by callosal fibers[8]. The two homologous areas connected by these latter anomalous tracts were exactly those in charge of intermanual transfer of object recognition (see Figure 2C and D). By studying this function behaviorally, as described above, we confirmed that the patients were indeed able to perform the task with the same competence of typical subjects.

Conclusion: At least some of the tracts formed by long-distance neuroplasticity, when a developmental perturbation hinders normal formation of the corpus callosum, are compensatory for some of the functions that would have been performed by the normal callosum. However, many of these patients show symptoms that may be as severe as mental retardation. So, our hypothesis is that the other anomalous tracts formed in the patients may not be compensatory, but harmful to them. These tracts are functional, as we also have shown[9], although we still do not know which function they perform. They convey a conversation between brain areas, so to say, but we do not know the subject. Thus, plasticity can be compensatory, but may also be maladaptive.

Maladaptive plasticity: About Schumann and Lord Nelson

There are some historical examples of presumably maladaptive plasticity, although at their time an explanation for the mechanisms was not yet available. The case of Robert Schumann (1810-1856), the famous German Romantic composer, is remarkable. Schumann started as a pianist, sharing this practice with his wife Clara Wieck (1819-1896). Both were taught by Clara's father, a very severe, demanding teacher who required many, many hours of training of his pupils per day. The result was the advent of serious pains in the hands of Clara, and a strange phenomenon in Schumann's. His third finger of the right hand turned rigid and lost most of the agile movements required for a pianist. Although attributed at the time to a mechanical device he had used to improve his performance, in fact his symptoms can now be associated to a condition called *focal dystonia*, known to appear occasionally in musicians and writers[10]. It turns out that the cerebral cortex and the corpus callosum undergo maladaptive plasticity caused by excessive use of the fingers. A reduction of the inhibitory influence of the corpus callosum on the hemisphere in charge of the affected hand caused a disorganization of Schumann's body map, as represented in the surface of the somatomotor cortex. As a result, finger movements failed to be appropriately coordinated.

The other historical example of maladaptive plasticity is that of Lord Horace Nelson (1758-1805), the famous British admiral who lost his right arm at the Battle of Tenerife against the Spaniards in 1797. After the trauma, he developed a strange symptom known as "phantom limb," which made him feel sensations as if they were coming from the lost limb: tingling feelings, itch, and also pain. Nobody knew how to explain the phenomenon at that time, and Nelson wrote about it to say that he had "found the direct existence of the soul."

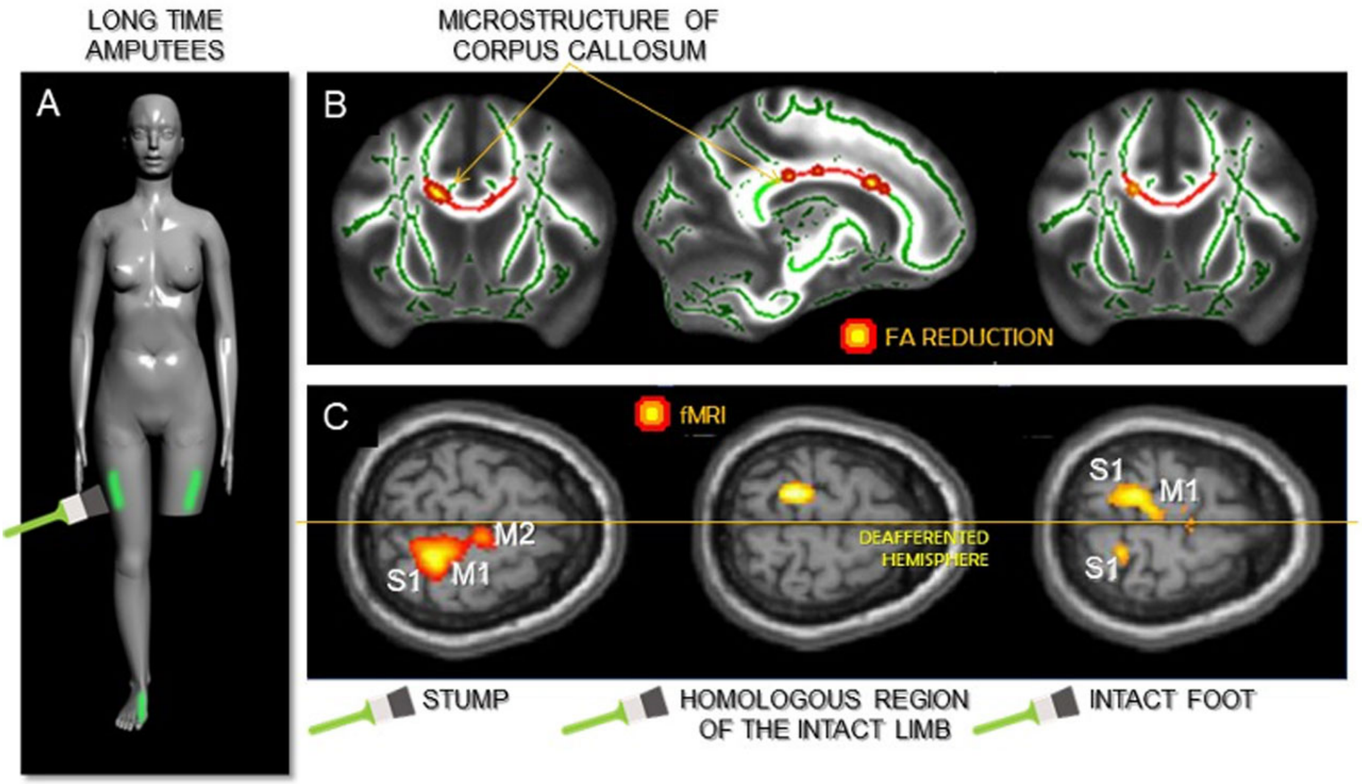

Figure 3. The brain of an amputee was studied by stimulating the legs with a brush (A) while imaging the structure of the corpus callosum (B) and the activity of touch and motor areas in the cerebral cortex (C). The callosum reveals microstructural disorganization, while the cortex reveals expansion of touch areas after stimulating the stump, as compared

with the result of stimulating the intact thigh and foot. FA = fractional anisotropy, a proxy of white matter microstructure. fMRI = functional magnetic resonance imaging. Modified from Simões and collaborators[11].

The phantom limb syndrome is more common than one may think, and occurs in the great majority of amputees, as much for the limbs as for other parts of the body. The result is great suffering for the patients. For this reason, we were interested in explaining this strange type of neuroplasticity and, with that purpose, we studied human lower limb amputees by using morphological and functional magnetic resonance imaging[11] (see Figure 3A). We found something similar to the cortical disarray described above for the focal dystonics: signs of disorganization of the corpus callosum microstructure (see Figure 3B), and changes in the representation of body parts on the surface of the cortical areas in charge of touch (S1 in Figure 3C) and motor control (M1 and M2 in the same Figure). We later confirmed that interhemispheric connectivity was greatly reduced while intrahemispheric connectivity was increased[12]. We also employed animal models to achieve more reductionistic explanations and concluded that, not only had the corpus callosum fibers lost part of their isolating sheath, but also that the fibers themselves were greatly altered at their terminal branches within their targets at the opposite hemisphere[13].

Transpersonal plasticity: The biological basis of education

Moving to a higher heuristic level of neuroplasticity as an explanation for education, we ought to examine what educational interactions consist of. They are a type of social interaction, by which someone exerts some actions planned to motivate, facilitate, or provoke someone else’s learning. There are two interacting parts: in general, one or some teachers, and some or many students. Although a unidirectional model of education still survives, as in old-fashioned and inefficient classical lectures to dozens of passive pupils, the tendency nowadays is to utilize the bidirectional models that explore a reciprocal interaction between the two sides—students and teachers. If we consider these interactions as products of a conversation between brains, it becomes of great scientific interest to know how this phenomenon occurs. And viewed from this angle, we may call it an example of transpersonal plasticity: the way one brain is able to change another brain by functional interaction at a distance.

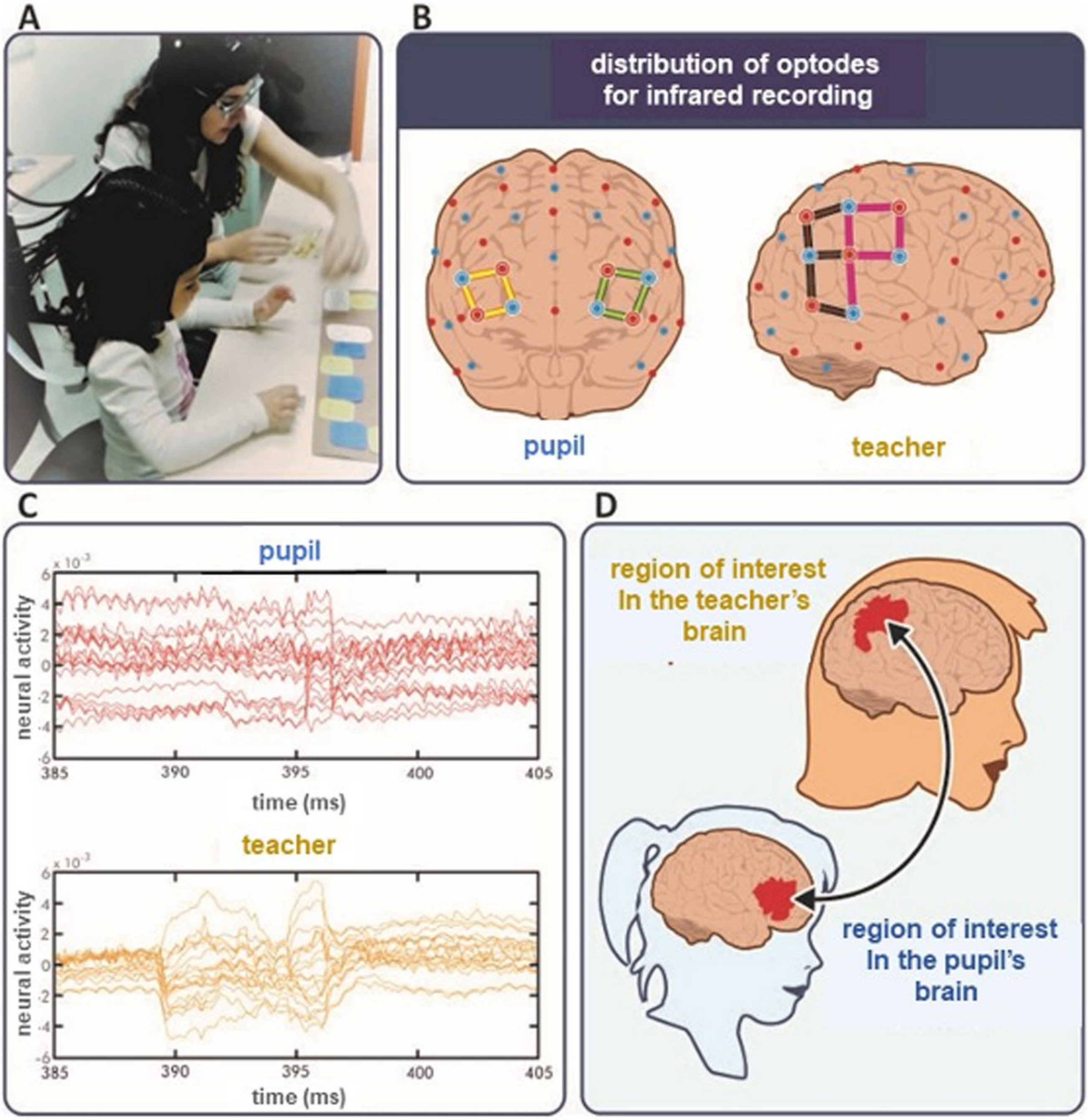

Figure 4. A hyperscanning experiment performed as a proof-of-concept for the use of near-infrared spectroscopy as a tool for studying transpersonal neuroplasticity. A shows the pupil learning how to sum two integers, with recording devices on the head to record their brain activity in synchrony (B-D). Modified from Brockington and collaborators[16] (illustration by Julio Xerfan).

The way to study this form of plasticity is to record the interacting brains at the same time using a naturalistic setup to simulate what goes on in a classroom. The first attempts with this purpose were not planned for an educational context but aimed to investigate how the activity of one brain impacts on another brain during some cognitive or emotional function.[14] More recently, techniques improved, and it became possible to develop very realistic settings and record simultaneously the brain of many students during learning activities. It has been possible to do it using the classical technique of electroencephalography (EEG), now perfected to yield spatially more accurate results, and by employing a new technique with the technical name of functional near-infrared spectroscopy (fNIRS). This approach became known as *hyperscanning* (see Figure 4).

A good, practical example of the first approach using EEG was the work done by David Poeppel and his collaborators in New York and Frankfurt[15]. They recorded the brain waves of 12 pupils from the second grade participating in class activities of various formats, conducted by the teacher during 11 sequential days. The activities consisted of listening to a text read by the teacher, attending a lecture, watching a video, and discussing as a group. The researchers could record brain wave synchrony between pairs of students, between each one and the group, and among the group as a whole. After the experiment, students evaluated the different pedagogical styles, and their preferences were related to the patterns of brain activity. The results were somehow obvious: Participative activities were preferred and more efficient, and the reason seems to be the collective attentional focus on the same target or objective. But things are not so simple, because synchrony between pairs of students revealed an influence of each one's learning preferences, and the individual ability to focus attention. The authors went further: They induced direct (face-to-face) and indirect (side-by-side) interactions and verified that the former produced a greater increase in brain synchrony during the pedagogic activities that followed in sequence. This provides decisive evidence that empathy between persons influences learning.

Similar experimental designs can now be used with a better spatial resolution to localize the regions of the brain active during teaching and learning, by employing fNIRS and combining it with other recording techniques such as eye-tracking and pupillometry[16], that measure the focus and degree of attention, respectively. I have participated in one such study (see Figure 4), performed as a proof-of-concept of the approach. Hyperscanning will perhaps mark the future of naturalistic approaches of transpersonal plasticity as a proxy of learning.

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[1] Parts of this text were based on my book *O Cérebro Aprendiz* (The Apprentice Brain, 138 pp.), published in 2019 by Editora Atheneu, Rio de Janeiro, Brazil.[1]