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FOREFRONT REVIEW

"Knock once for yes, twice for no"

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Abstract Previous studies have indicated that the expression of CCN3, a member of the CCN family of proteins, was tightly regulated during central nervous development and was associated with acquisition of cognitive functions in rats (Perbal, Mol Pathol 54(2):57–79, 2001; Su et al. Sheng Li Xue Bao 52(4):290–294, 2000) therefore suggesting that CCN3 might be involved in higher levels of physiological communication in the brain. In spite of the considerable amount of progress made into the understanding of neuronal organization and communication, reducing the knowledge gap between brain cellular biology and behavioral studies remains a huge challenge. Mind-to-mind communication has been the subject of numerous science fiction writings, intense research and emotional debates for many years. Scientists have tried for a long time to achieve transmission of messages between living subjects via non intrusive protocols. Thanks to the great progress made in imagery and neurosciences, another dimension of neuronal function in communication has now been documented. Two recent experimental demonstrations of direct brain to brain communication without physical contact (Grau et al. (2014) Conscious brain-to-brain communication in humans using non-invasive technologies. PLoS One. Aug 19;9(8)- - Rao et al. (2014) A direct brain-to-brain interface in humans. PLoS One. Nov 5;9(11)) pave the road to more sophisticated applications that could profoundly affect communications of humans with other humans, animals and machines. Although the wide use of such applications might seem a long way off, they raise quite a number of ethical, legal and societal issues.

Keywords Neuroscience · Communication · Brain research · Brain-to-brain interface · Brain-to-machine communication · Direct human brain-to-brain communication · Human-to-animals communication · Mind-to-mind communication · Cognitive functions · Brain initiative · HBP project · Minds project · Connectome

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The brain projects

The huge interest that has developed at an amazing pace for the field of neurosciences over the past few years is illustrated by the US Brain Research, Advancing Innovative Neurotechnologies (BRAIN) Initiative,[1] and the Human Brain Project (HBP),[2] that were launched in 2013, followed in 2014 by the Japanese Brain/MINDS[3] project.

The aims of each of the individual projects and the approaches are quite different.

While the American project focuses on establishing a map of all neuron connections (« connectome ») in the human brain, the European approach aims to create a « virtual brain » by connecting large computer networks through cloud technology.

The Japanese program is devoted to deciphering brain circuitry in animals and humans, with the hope of applying new findings to the treatment of human mental illness.

Although the promises are great, expectations should be kept at a realistic level.

First, it is important to consider scientific criticisms regarding the biological significance of creating a static map of the brain cell connections when functioning of the brain involves a tremendous level of plasticity in the neural connections.[4] In spite of the great knowledge that has been accumulated

[1] http://www.kavlifoundation.org/kavli-news/brain-initiative
[2] https://www.humanbrainproject.eu/en
[3] http://brainminds.jp/en/
[4] Are we living in the age of the brain? By Phillip Ball in December 22, 2014 issue of Prospect, the magazine of leading ideas.http://www.prospectmagazine.co.uk/blogs/philip-ball/are-we-living-in-the-age-of-the-brain

through the study of the C . elegans connectome (connective map of the 302 C. elegans neurons), it appears that the functional expectations regarding relationships that could be drawn between behavior traits and neuronal maps might not be met and are the subject of intense debate.[5] Recent work established that modularity is not sufficient to account for the connection specificity of such networks (Kim and Kaiser, 2014).

Second, it seems that running these big collaborative projects is not an easy task, as shown by the alarming message sent by members of the European neuroscience community to the European commission[6] regarding the « overly narrow approach » of the human brain project that lead to a « significant risk that it would not reach its objectives ».

Third, it is essential to convey realistic messages. We all remember those colleagues who claimed that sequencing of the human genome would provide a rapid understanding of mental illness, behavioral problems[4] and eternal life (see JCCS editorial, B. Perbal, 2014) ! The same was conveyed over the past three decades in the cancer field, about oncogenes, telomerase, tumor suppressors and many more « extraordinary discoveries » that made the front pages of journals.

The sole collection of a huge amount of data is not likely to be sufficient to provide the keys to brain function understanding. We have no clue, at the present time, about the way information is organized and integrated in and by the neuronal networks.

As discussed elsewhere[4] brain and computational activities might share common ways of networking. However, the central question, that cannot be eluded, is to determine what kind of a computer should the brain be compared with, if any.

What if brain is not simply working as sophisticated artificial networks that are supposed to mimic its organization and functioning ?

Objectivity and humility are required.

Brain electrical activity and behavior

How brain controls human communication has always been a fascinating question for both the scientific community and the general public.

Science fiction has embraced the subject of inter-brain communication in many instances and for years.

Telepathy has been and still is a major topic of discussion and argumentation…

How do the neural connective networks govern human emotions, thinking, imagination, behavior ? What is the basis of mental illness ? Will our knowledge of brain cell functioning lead to effective therapies ? Central questions, among many others, for the fate of humanity.

How the electrical activity of the brain relates to behavioral responses and affects cognitive functions has been studied for many years and has led to a considerable amount of literature.

Brain stimulation by local current applications, which was introduced in the 19th century by L. Galvani and A. Volta, has come to the front scene again with the emergence of brain imaging techniques (quoted in Trimper et al. 2014).

Transcranial direct-current stimulation (TDCS) delivers a constant low current to limited and well defined brain areas (see a review of electrical brain stimulation techniques by Ruffini et al. 2013). TDCS has been reported to help patients with various brain injuries, although recent studies might trigger a more critical interpretation of published results.[7]

As soon as a well defined and controlled delivery of current to the brain was reported to increase cognitive performance, to help fight depression and enhance memory in healthy subjects, commercial devices soon became available on the internet, thereby providing aids that could turn out to be more deleterious than helpful.[8] Caution is critical.

The identification of brain regions related to particular functions, the development of imaging technologies, and the ability to record neuronal electrical activities, all provided the means to translate the « biological currents » emitted by neuronal networks as signals used to operate external devices through non-invasive technologies.

Brain-machine interfaces (BMIs) have been developed that use the recording of neuronal activity to command external devices such as prosthetic limbs in very sophisticated ways.

Somatosensory feedback, is essential to prosthetic sensation. Implementation of a brain-machine-brain (BMBI) interface by intracortical microstimulation (ICMS) of primary somatosensory cortex permitted the demonstration of bidirectional communication between a primate (monkey) brain and an external mechanical device (O'Doherty et al. 2011).

A next step consisted in transferring motor or sensory information generated in the brain of an « encoder » rat to that of a « decoder » rat. The transfer of information was performed either from adjacent cages or via internet to a rat located in Brazil. In both cases, tasks were performed successfully by the decoder rat (Pais-Vieira et al. 2013, cited in Trimper et al. 2014). Further experimentation indicated that cognitive information could also be transfered from one animal brain to another (Deadwyler et al. 2013, cited in Trimper et al. 2014).

[5] The Connectome Debate: Is Mapping the Mind of a Worm Worth It? 2012 Scientific American. http://www.scientificamerican.com/article/c-elegans-connectome/?print=true

[6] see Open message to the European Commission concerning the Human Brain Project. http://www.neurofuture.eu/

[7] Brain Hackers Beware: Scientist Says tDCS Has No Effect. http://spectrum.ieee.org/biomedical/ethics/brain-hackers-beware-scientist-says-tdcs-has-no-effect

[8] Warning over electrical brain stimulation. http://www.bbc.com/news/health-27343047?print=true

Human to rat non-invasive brain communication was performed through the combination of human scalp-derived EEG[9] on the brain-computer interface (BCI) side (emitter), and ultrasound brain stimulation on the computer-brain interface (CBI) side (receiver) (Yoo et al. 2013). The signals captured from the human scalp were transferred as signals evoking tail movement in an anesthetized rat.

Direct brain to brain communication

Publications from two independent groups in PLOS (Grau et al. 2014,[10] Rao et al. 2014[11]) constitute an important step forward, as they reported non-invasive brain to brain communication between humans.

Unproperly qualified as « telepathic » communication in the press, these two reports demonstrate that direct brain to brain communication between two physically distant humans can efficiently take place remotely through the internet network.

In the Grau et al' (2014) experiments, the BCI emitter subject was located in Thiruvananthapuram, India and the CBI receiver was located in Strasbourg, France.

The EEG information corresponding to the simple greating words « hola[12] » and « ciao[13] » were encoded in the form of a digital binary code series of « O » and « 1 » and sent from the BCI interface by internet. At the receiver end, the message was delivered to the subjects via robotized transcranial magnetic stimulation (TMS).

The receiver subjects who did not hear nor see the words that were transmitted by email, could properly report the perception of TMS induced phosphenes corresponding to the message sent, thereby confirming the feasibility of conscious mind to mind transmission between two subjects via noninvasive technologies.

In their manuscript, Rao et al. (2014) report a similar type of direct human brain to brain interface between two subjects located in different parts of the Washington University campus.

On the receiver side, the subject was wearing a swim cap above which a TMS device was placed to stimulate the brain motor cortex region that controls hand movements.

On the emitter side, the other subject was connected to a device detecting motor imagery EEG signals that corresponded to brain activity.

Upon completion of the internet signal transmission, decoding by the receiver of the messages sent by emitter resulted in the demonstration of a direct brain to brain communication that permitted two physically distant subjects to cooperate and achieve a desired goal in a computer game.

These results confirmed and extended observations of a pilot study that was « designed by the same group to demonstrate that it is possible to send information extracted from one brain directly to another brain, allowing the first subject to cause a desired response in the second subject through direct brain-to-brain communication ».[14]

It is tempting to imagine the impact that these new scientific advancements might have on our daily life. In an « internet of things » world, direct human-to-machine communication opens a great number of possible applications in our social and professional life, at home, at work, for both leisure and improvement of environmental quality. Human-to-animal brain communication would certainly also be the matter of a profound change in our relationships with pets but also, for example, with wild animals whose behavior is studied in national reservations or in a natural context.

Of course, the human-to-human direct brain communication would probably lead as the most sensitive aspect, due to the numerous applications that might come out of these kind of studies, for the best and for the worst of human societies …

Even though it remains that « communication is the key » (Perbal, 2014), the transfer of information between two brains raises several ethical and safety concerns. For example, the warnings expressed by security experts regarding the possible hacking of pacemakers by terrorists (Clery 2015), as shown in an episode of the TV series 'Homeland', would constitute a very sensitive issue in a wireless direct brain-to-machine communication context.. Readers interested in these aspects should consult the inspiring review by Trimper et al. (2014) in which the authors analyze some of the ethical implications that are expected to arise with the development of brain to brain interfacing technologies. Legal issues are among those which should not be set aside due to a lack of fast responses from agencies.

Societal consequences might go far beyond what is presently envisioned and should be careful considered in the near future.

Perspectives

In a world where people want to communicate information about themselves, about their lives, about their aspirations, about their problems and much more, the potential societal impact of non invasive « mind to mind » communication is huge and cannot be set aside to be addressed by the next generations.

Just as I believe that we should let people decide what they want to do with the genetic information that they own (Perbal,

[9] EEG here is imagery-controlled electroencephalographic changes
[10] submitted may 28, 2014, published August 19, 2014
[11] submitted July 21, 2014, published November 5, 2014
[12] « hola » is « hello » in Catalan and Spanish
[13] « ciao » is « good bye » or « hello » in Italian

[14] Direct Brain-to-Brain Communication in Humans: A Pilot Study August 12, 2013 http://homes.cs.washington.edu/~rao/brain2brain/experiment.html

2014), I do not think that it would be reasonable to avoid wide applications of inter-brain and brain to machine communications.

Every scientific progress has been the source of good and bad applications. Whether this can be avoided in a satisfactory way for all concerned parties is presently an open question.

Establishing rigid frames, to avoid officially-uncontrolled developments, has resulted in hidden side-achievements that often end up being more dangerous than if they had been permitted and therefore visible.

Again I am confident that the only way to avoid witnessing dramatic situations is to stimulate, whenever it is possible, truly open discussions involving researchers, patients, physicians, legal representative, and industries.

Hopefully, humans will be wise enough, and the new era of open mind-to-mind communication will end up becoming « one giant leap for mankind »[15]

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