Practical Work
Neuroimaging as Big Data in the Cloud

Intelligent Data Analysis and Data Mining

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1. Introduction

The brain can be considered to be the most important organ in human body, if such ranking of importance is allowed, given that all organs are critical to survival. This importance not only comes from the fact that it orchestrates the functional processes within the human body, but also, and more importantly, from the fact that it is what makes us human, by allowing us to think and feel. Given this importance, it has been one of the priorities of the scientific community to investigate the mysteries of the brain. A very well funded european-wide project, namely Human Brain Project, or the U.S. version of it, the BRAIN initiative, which are dedicated to investigate the wonders and mysteries of the human brain, demonstrate the importance given to brain research.

From a “data” perspective, it is true that the brain creates information all the time, producing thoughts, knowledge, experience, sensations, sending orders to other organs, etc. but what interests neuroscientists more is the brain as data itself. The complex structure of the brain with different types of tissues and connections, which is still far from fully discovered, is one aspect of this data. Another aspect is the chemical and electrical processes, constantly taking place, throughout the brain, from birth to death.

In this study, I will analyze the challenges to obtain brain data in neuroscience; the effects and implications of it becoming “big data” on research; the barriers to the exploitation of it especially with new groundbreaking machine learning techniques; the “cloud” as a possible solution to remove these barriers; and possible implementation criteria of this hypothetical cloud. I will base my analysis mainly on MRI data, but it can also be applicable to other neuroscience data such as EEG and MEG.

2. NeuroImaging

There are so many conditions or diseases originating from or affecting the brain, which are related to physical, physiological, or psychological functioning of the body, that it is very critical for human life to be able to observe the brain as data itself and extract information from it. This data ideally should give us information on what abnormality there is from the norm, where it is stemming from, how it is progressing, etc. It is important to understand the brain, not only from the perspective of abnormalities, but also to be able to grasp the nature of normal human behaviours, feelings, bodily processes because a grand majority of these are brain-originated.

The brain is such a delicate organ and therefore protected by nature with such a strong case that it has been always difficult, limited and risky to analyse the brain invasively on a living human body. There has always been a need for being able to examine the brain structure and processes non-invasively. Thankfully, recent advances in science have made it possible to develop techniques to investigate the brain in a non-invasive fashion. Now we have a range of techniques which allow us to throw a different light on brain and study a different aspect of it. Here are some of the techniques commonly used in neuroscience to throw light on the structure and inner workings of the brain, which produce the big bulk of the neuroscience data:

EEG: Electroencephalography (EEG) is a technique to measure and record the electrical activity of the brain. EEG measures the electrical activity of the brain over a period of time, with the help of electrodes placed on scalp, which capture voltage fluctuations within the neurons of the brain and send them as signals to a specialized computer where these signals are recorded. EEG is used to detect abnormalities in the normal electrical activity of the brain in the diagnosis of conditions or diseases like epilepsy, sleep disorders, coma, stroke, etc. It has very limited spatial resolution but very fine temporal resolution.

PET: Positron Emission Tomography is a technique based on nuclear processes that measures the metabolic processes in the body. The technique works by detecting gamma-rays emitted by a tracer molecule introduced into the body, which then constructs a three dimensional image of the concentration of the molecule throughout the body. It is mainly used in oncology to detect tumors and metastases.

MEG: Magnetoencephalography (MEG) is a technique to measure brain activity by detecting the magnetic field produced by the electrical current in the brain. The technique may be used to detect the abnormalities in the brain by the changes in the magnetic field or may simply be used in experimental settings to observe the magnetic/electrical activity of the brain.

MRI: Magnetic Resonance Imaging (MRI) is a medical imaging technique to form pictures of the anatomy and medical processes of the body, which make use of magnetic fields, radio waves or field gradients. MRI is a very powerful technology in neuroscience allowing to investigate the details of human brain in various perspectives. It is so flexible in the sense that one can measure the macrostructural features of the brain (such as cortex thickness or volumes of different sub-structures), microstructural features (such as diffusion within white matter tracts) or functional activations in the brain (task-driven activations or resting state properties). The scale of the MRI image data may vary depending on the modality and the resolution used. MRI can be considered under three categories, structural MRI, functional MRI and diffusion MRI.

sMRI: sMRI provides the static anatomical information, such as the size and shape of the white and gray matter. In structural MRI, different structures appear in different levels of contrast. It is used to observe the structural abnormalities in the brain, such as tumors, lesions, etc. It has several modalities, such as T1, T2 and FLAIR (See Figure 1.).

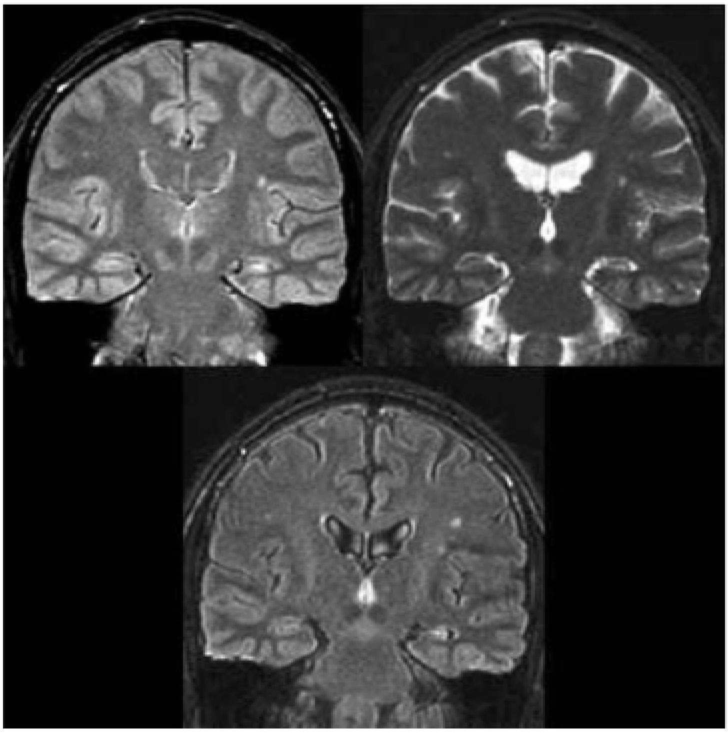

Figure 1 - Different modalities of sMRI [11]

fMRI: Functional MRI (fMRI) measures indirectly the brain activity by directly measuring the oxygenation level of blood throughout the brain. The main aim of this technique is to find a relationship between structure and function. The scanning is typically accompanied with a behavioural task and it is done taking many scans through time within a short time period. Thus, the resulting data is a 4D image, which is converted to a 3D contrast image.

Diffusion MRI: In this scanning technique the relative motion of water through each voxel in different directions is captured. A tensor analysis is carried out to calculate the direction and the intensity of the motion through each voxel. Since it is known that water moves more easily along axons than across them, this technique mainly gives information about the connectivity throughout the brain. The abnormality in the connections may indicate a structural or functional abnormality in the brain, such as tumors.

3. Data Understanding

Neuroimaging techniques are generally based on special scanners of the brain, which turn tissue properties into volume-elements(voxels) in certain resolutions. This scan can be carried out in different orientations (radiological, neurological), in varying dimensions (2D,3D,4D), in different spatial and temporal resolutions. These data are generally stored in a raw binary format consisting of either 8- or 16- bit integers. Along with this raw data, there is also usually the metadata including the descriptive information such as, subject information, type of image, imaging parameters and image dimensions.

Even though these neuroimaging techniques are non-invasive, they can cause some level of disturbance to the patient. For instance, they require the patient to stay still in a certain position until the scanning is complete. This also poses a problem to the standardness of the data, which is specifically important for automatic techniques, because it is never possible to fix the head in a certain position without any movement.

The possible potential side effects, which are still to be investigated, is another issue in the usage of these techniques. The doctors look for a valid reason to require the patient to go through a scan in order not to subject him to unnecessary disturbance and danger. Moreover, the scanning process does not come cheap, require special machines, equipment, staff and therefore is prescribed with parsimony. For these reasons, the data does not abound, which is important in data mining and machine learning techniques.

Each of these scanning techniques measure different indicators and one cannot in general be converted into the other. Therefore, even though they are all images from the brain, they provide a different kind of information on brain and need to considered in different categories. Besides the obvious differences between different techniques, there is also variation within the same scanning technique. For one given technique, there might be several modalities, different machines, different resolutions, image quality, etc and this causes problems in the standardness of the data. This might look like a problem at first look but it is also an advantage to have different information types on brain, which is exploited more and more in research under the name multi-modality.

Because of all this variation in brain data, it is crucial to bring them to similar distributions using some pre-processing techniques. Skull-stripping (removing the skull from images), field-bias correcting (removing the undesired signal from images), motion correction (removing the effects of the movement of the head in different images and aligning them to the same space), intensity normalization such as 0-mean unit variance standardization or histogram normalization are the common pre-processing steps applied to brain images to obtain similar distributions.

4. Big Data in Neuroscience

In spite of the difficulties, risks and cost of neuroimaging techniques, the data is becoming more abundant, precise, complex and varied in neuroscience thanks to the accumulation of data and technological advances. Now neuro-imagers collect more data in a few days than that was collected over a year a decade ago. Finer spatial and temporal resolution is achieved with better MR technologies. There are also different modalities in a single technique, such as T1, T2 and FLAIR (see figure 1) in structural MRI, each of which reflect the brain in a different light. It is possible now to say that neuroimaging is officially a “big data” science. In the context of neuroscience the term “big data” implies data size, complexity and modalities.

Up to a recent past, this neuroimaging data was mainly inspected by human experts. The problem with manual inspection methods is that they require experts, they are time-consuming and susceptible to the limitations of human judgement, therefore, subject to inter- and intra-expert variability. For example, Multiple Sclerosis (MS) lesion segmentation task on MRI images may produce different results with different experts as well as with the same expert at different times. Besides, even one MRI segmentation may require hours of valuable expert time. There is a great need for semi-automatic and fully-automatic techniques to help the experts and even obviate the need for these experts, while at the same time bringing more consistency and reliability.

Thankfully, the fields of machine learning and data mining are going through a revolution in the past years. Although they are not recent fields, with the accumulation of the data and development of new techniques, they have started to produce very promising and convincing results. Neuroimaging is one of the areas where machine learning techniques are heavily being applied to find automatic solutions to diagnosis and prognosis of certain brain-related disorders. Moreover, these techniques are capable of learning from data, especially when a clear definition can not be made of the problem at hand. For example, in manual MS lesion segmentation, the experts use their intuition together with their knowledge to perform the task. However, machine learning algorithms, if trained with the correct algorithm and enough data, can learn correctly the relation between a region of the brain and whether it is a lesion or not.

From among these techniques, deep learning has stood out recently with very successful results in neuroimaging problems. It is possible now to see a lot of research on the application of convolutional neural networks (CNNs) or other deep learning techniques on lesion segmentation tasks for diseases like MS or Alzheimer's. These techniques are capable of representing very complex functions and are capable of extracting useful features from data, eliminating the initial step to design features. To give an example to one such application, one CNN implementation [10] with several layers was the winner of 2015 MS Challenge (see Figure 2). Given such successful results they become more and more popular.

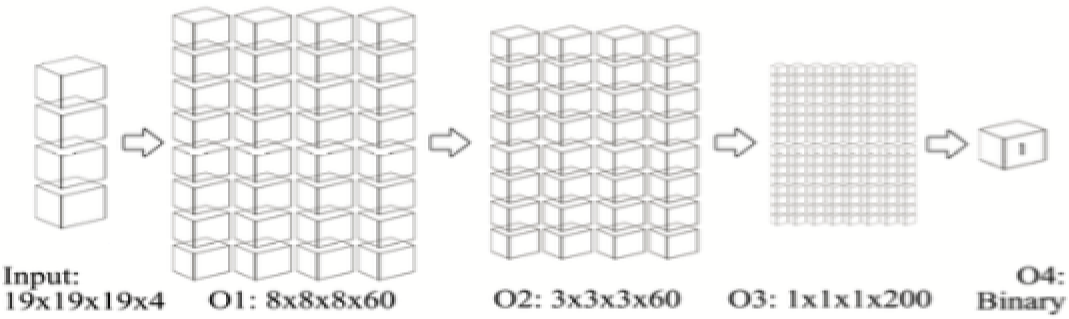

Figure 2 - The winning CNN architecture in 2015 MS Challenge [10]

However, these techniques come with their own problems. They require a lot of data to generalize well and consume a lot of processing power. Especially in the case of neuroimaging problems, these problems are more pronounced. Considering, for example, the lesion segmentation task, the classification is done for each voxel in an MRI image with a feature vector of tens or hundreds of features (surrounding voxel values). As feature vector size grows, especially if the underlying function is rather complex, the need for more data and more complex network designs increases in order to generalize well, which in turn require more space and more processing power. And this is exactly the case for many neuroimaging problems. Moreover, in tasks such as lesion segmentation, the labeled data is only a small proportion of the whole data available. With supervised machine learning techniques, the acquisition of such labeled data is crucial.

With the limited amount of data and limited processing power, reproducibility and reliability of the results are a big concern in research. Reproducibility is defined as the ability to replicate the same results both with an analysis pipeline on different datasets and different analysis pipelines on the same dataset. Low statistical power of research results puts into question the reliability of the research findings.

The accumulating data and ever growing power of computers alleviate these problems to a certain extent. With more amount of data and better designed experiments, it will be possible to obtain reliable and universal findings. However, still many limitations exist. The data that can be accessed by individual researchers is still a fraction of what is available and personal computers are still not strong enough to handle complex machine learning techniques efficiently.

5. Cloud for Neuroscience

Up to recent past, the data accumulated by individual researchers or institutions mostly resided on the hard-drives within their laboratories and was not shared or catalogued due to commercial worries, privacy and confidentiality reasons. Moreover, even if the will to share existed, there was not common repositories to share the data and, therefore, when one researcher needed data for his research, it was not clear where to turn to and which procedures to follow to obtain the necessary data. In fact, the totality of all these small-scale datasets comprise the long-tail of the neuroscience data, since, even though they are small they comprise the majority of all data in total [4](see figure 3).

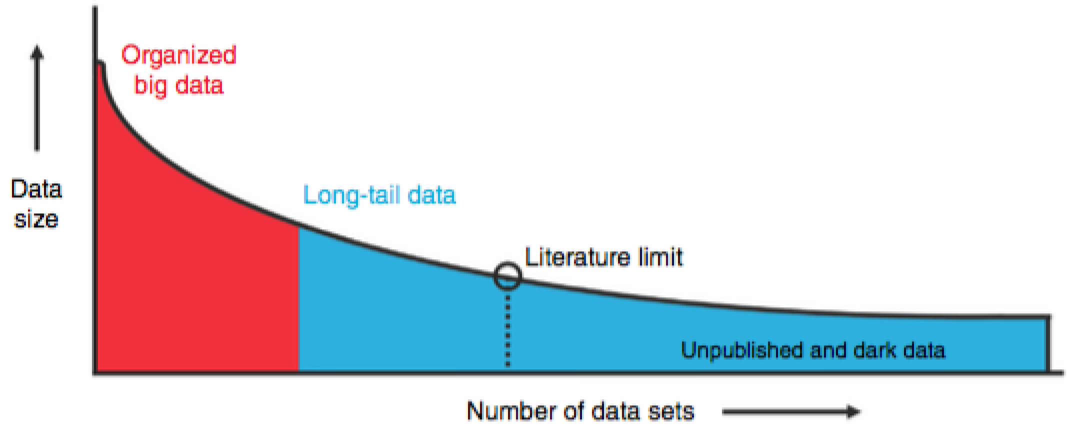

Figure 3 - The distribution of different sized datasets in neuroscience [4]

Given the reality of “big data” waiting to be tapped, neuroimaging is recently going through a revolution in open-access data sharing and some neuroimaging databasing attempts are being undertaken to alleviate the common need for data. One very important development took place recently, which would be a strong candidate to answer the challenges in benefiting from “big data” in neuroscience: Cloud technologies. Cloud technologies allow depositing data and services on remote servers removing the need to keep or have the data locally. Huge amounts of data can be stored and accessed via these remote servers, which eliminates the need to invest in expensive hardware. Besides storing the data, cloud technologies also offer to process the data as needed in these remote servers by providing strong processors and dedicated software. This is also known as “software as a service” meaning that it is no longer necessary to install softwares locally because they can be activated and run on a remote fashion on remote servers.

Think about the advantages of these technologies for neuroscience. Steps to carry out an experiment in neuroscience would normally include collecting data from different sources, understanding the data, installing the necessary software to standardize the data, installing the necessary tools to set up the experiment, making sure that the dependencies are installed, installing other software to visualise the data. All these steps are done in different fashions without guidance or enforcement on general standards and sometimes with unreliable or erroneous results. The data collected is limited and in varying formats and qualities. Technical expertise is required all the time to install a software, configure it and learn to use it. Moreover, the efforts made to standardize the data and apply the software are not transferred and partly lost.

One of the advantages cloud technologies would bring is the collection of data in one place or in several common repositories. With this achieved, the access to data would only be a matter of registration and having the access rights. There are already some small scale efforts in collecting brain data under one roof, mostly related with a specific disease like Parkinson’s, psychiatric disorders, autism, brain injury, etc. Examples include XNAT central in Human Connectome Project, Alzheimer’s Disease Neuroimaging Initiative(ADNI), NIH-based National Database of Autism Research(NDAR), Federal Interagency Traumatic Brain Injury Research(FITBIR), the SumsDB effort for cortical surface-based atlasing of neuroimaging results and NIH MRI Study of Normal Human Brain Development containing neuroimaging data of children between ages 6 and 18. The main aim of all these efforts is to facilitate the cooperation across centers and disciplines to integrate and access data. Although these efforts only represent a small fraction of the “big data” in question, they are a huge step in having a more centralized and comprehensive solution to store and share the data.

One other advantage of the cloud would be the shared software. The cloud offers the keeping and running software on remote servers, which is also known as “software as a service”. This software can be for standardization purposes (data pre-processing), for applying standard or customized machine learning algorithms (modelling) or for analysis and visualization purposes. The experimenter need not worry about the purchase, installation, the storage of the software. Thus, the need for space and expertise would be partly eliminated.

The cloud also offers distributed processing power, which eliminates the need for investment in powerful machines to run complex and resource-intensive machine learning algorithms or to run applications for analysis and visualisation. The usage of powerful processors and Graphics Processing Units (GPUs) enable parallel processing and increase efficiency. There are already commercial cloud solutions in place for this purpose, such as Amazon AWS to provide processing power in return for a reasonable fee. These services even provide application environments to develop machine learning algorithms, which eliminates the need to install them on local computers.

6. Implementation

Many questions arise with “big data” in the “cloud” such as how to store the data efficiently, how to share it safely, how to determine common standards, how to share software, how to allocate processing power, etc. Recently many individual and unconnected attempts have been undertaken to resolve these challenges. There exist data repositories from which data can be downloaded for use in research, some data standards already exist for several domains of neuroscience, software code can be shared via publicly accessible repositories (e.g. github), algorithms can be run in the cloud on commercial service providers (e.g. amazon aws), there exists various approaches to make the data available (sharing via FTP sites, the secureness of which is debated, or federated archiving approaches, according to which data remains local but the participating institutions may access each other’s data via agreements)

All these models have their own challenges in data storage and management, and they are far from being unified, central and coherent. However, it is possible to design a “neuroscience cloud”, where all these individual efforts are considered in connection with and dependent on each other, centralized and managed coherently. This “neuroscience cloud” would be like a giant computer system on which data, standards, code, processing power and analytical results are brought together.

First of all, this system should be democratised in the sense that it should be open to data contributions, ideas, software, analysis results and access from the whole of scientific community. This way sharing is encouraged because everyone can contribute and get some benefit from such sharing. To incentivize the data contribution, the long term benefits should be understood and appreciated by the scientific community. The Belmont report, which provides a framework for human subjects research in the United States, stipulate that the researchers have a duty to maximise the benefit to the science while at the same time minimising the harm to subjects [3]. It must be thus considered an ethical duty on the part of researchers to share data unless doing so increases potential harm to subjects.

Although sharing data entails certain risks to subjects, it is possible to remove some of them making it ethically impossible to refuse to share in many cases. Researchers also fear that if they make their data public, they will not be credited by their efforts in obtaining or collecting the data. In such cases, to give credit for these efforts, new measures such as including the data owners as coauthors in any paper published on that data or allowing the publication of "data papers" which would then be cited in papers using the data, should also be introduced.

There must also be a mechanism and sufficient controls to enable storing of private and confidential data. Private data should be allowed to be stored in a secure way and be accessed only with authorization. Access controls should be flexible enough to satisfy every sharing needs. It is understandable that some data may contain information on subjects, that is potentially risky to make public, but cloud can provide the sufficient security to store such data while at the same time giving the same benefits to the authorized parties. The usage and sharing should be carefully controlled by clearly defined conditions agreed by providers and consumers. Pooling data from different resources, harmonizing them and authorizing access have to be managed efficiently and with caution; legal and ethical concerns need to be addressed for common storage and sharing solutions.

With bulk storage comes the question of efficiency. Hosting, managing and curating the data should be made efficient to enable fast upload and download. The data needs to be indexed, catalogued, tagged efficiently to enable fast access to relevant data. It is crucial to make the repository as organized as possible to allow for the arrival of the new data as well as efficient and correct access to available data. The storage need not be in one physical location, it can be designed as a distributed system, it can even be designed as a collection of institutional or individual repositories brought together with correct identifiers and reference systems. The softwares handling the ever-growing data need to employ better optimised algorithm to keep up with the growing size. The already existing data storage and sharing facilities (e.g. figshare) can be taken as a model to resolve the technical challenges.

The system should support a wide range of data - differing in complexity, scale and modality - but also establish some standards in the format and quality of the data. Having common standards enables intra- and interdisciplinary interaction encouraging research and development. Standard acquisition is also important because there are differences in acquisition rates, resolutions, scanning parameters, etc across different machines. These standards should be as flexible as possible not to deter people from contributing and to make the system adaptable to the new information. Instead of imposing unnecessary standards, it is also possible to subject the data to some pre-processing methods to keep it in line with the common standards. In order to really benefit from “big data”, standards to obtain, handle, store, convert, and pre-process need to be established.

The importance of metadata, which contains the information about how they were acquired, what transformations they went through, information about the subject to which the data belongs, should be emphasized in such a system. This part of the data is a guide to understand the data and put it to appropriate usage. The metadata should conform to common standards, it should be understandable and searchable by every researcher. Standards like XCEDE and NIDM already accepted by the scientific community could be modeled upon to agree on the general needs for the metadata.

The system should allow and encourage the sharing of algorithms and software code for purposes such as upload, download, preprocessing, analysis, managing usage rights, development environments, visualization etc. This way existing research could be reproduced on new datasets, adapted to different needs with slight changes or built upon and improved. Sharing of machine learning and data mining algorithms are particularly important, since they will be used extensively across different experiments. Some coding and quality standards, similar to sckitlearn standards, could be proposed even though it would be difficult to ensure these standards. This could be seen as an open source project, the successful examples of which we have seen so far, such as the operating system Linux. The code should be able to run on other cloud systems or individual computers to ensure the portability and flexibility according to personal needs. For sure, there will always be custom software on the part of the client to be run on data. In such cases, the cloud can be used for processing purposes or even for the development of the algorithm. The client should be able to develop or run whatever algorithm it chooses in distributed systems offered by the cloud.

Since individual computers are not suitable to analyze the available amount of data, for large-scale analysis of the neuroimaging data, distributed processing elements are needed. It may not be possible for researchers to obtain the necessary processing power and even if possible, it would not be efficient to invest in it on an individual basis. The processing power, especially with GPUs for more efficiency, should be provided on the cloud. This service can be offered by commercial providers on the cloud in return for fees per use. For instance, agreements with companies such as amazon, which already offer services like Amazon Web Services(AWS) providing processing power, storage and deep learning environment in return for a fee, can be made. It would not be possible to make this service free because there would be maintenance costs and also some controls on unnecessary usage would be needed. However, making it available to everyone on the cloud environment and the economies of scale would decrease the costs to the service providers making it affordable for everyone.

A new operating system should be designed specifically for the cloud to run all the services, from uploading and managing the data to running analysis to visualising the results. This together with distributed processing will allow the usage of the services from any type of device at hand. The design can be carried out by a team of architects considering the diverse needs of the cloud. The cost can be covered by government contributions, research funds or other donations.

For the storage costs of the public data, small contributions may be required from people who are benefiting from the data or the system as a whole. For the private data storage, the cost should belong to the owner of the data. In both cases, the economies of scale would make the costs lower than the amount expected without a cloud solution.

The education and increased awareness is very important for the acceptance and the maintenance of such a system. First of all, the scientific community should be convinced that it is necessary, viable and in their long-term interests. It is important to understand the needs of the general community and allow everyone to contribute ideas in the initial stages of the implementation. If scientists see the long-term benefit, they will be willing to make small sacrifices. There will also be need for different roles in the implementation and maintenance of the whole cloud system. Architects, to design the infrastructure, application developers, to contribute applications, data scientists, to contribute algorithms, educators, to increase awareness and to train the other roles will be crucial in the viability of the cloud system. New educational strategies need to be adopted from undergraduate to postdoctoral levels to train neuroscientists proficient in data mining, machine learning and cloud technologies.

7. Conclusion

It is obvious to see the benefits that would be produced with the application of this “big data” to the accumulating knowledge in data mining/machine learning. If the challenges are addressed properly, the gains from “big data” in the cloud would be enormous. With the usage of cloud in storing and sharing data, the cost and effort to obtain data would be minimized. More data will mean better designed experiments and better quality in the results. The collection of highly varied data under the cloud would also enable the adoption of certain standards. The standards that are better and more popular will prevail while weaker ones will be eliminated.

Moreover, the shared software and the access to more and better standardized data will enable more sophisticated machine learning algorithms to be applied to data. With cloud technologies, a wide variety of useful software and more processing power will be within reach of the researchers, who would in turn design more sophisticated experiments without the fear of overfitting. The results will be obtained much quicker and necessary tuning would be realised for better results.

With the barriers removed, the incentive to do research will increase substantially. More research with more and better data will bring increased reliability and the reproducibility of the findings in the research undertaken. Moreover, the results will be compared and cross-checked more often with increasing research improving the results further. Thus, new discoveries in brain science will be accelerated, which would mean improvement in public health and savings in health expenditures for the government.

However, for all its benefits, the design and implementation of such a cloud system for neuroscience will not be an easy task and will present many challenges, such as privacy, data ownership, infrastructure, governance, financial, legal and ethical concerns, etc. In this study I tried to present a possible scenario with which to make this cloud a reality. Many improvements can be proposed to this scenario but I believe, if these challenges are addressed correctly, it is feasible to obtain a Neuroscience cloud with the necessary will of the whole community, which will bring huge benefits in the service of humanity.

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