

The technology transfer in Healthcare 4.0: the use of Machine Learning solutions for neurodegenerative diseases

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Abstract. Artificial intelligence has the potential to revolutionize healthcare and machine learning approaches are able to be the catalyst for transformation of health systems to improve efficiency and effectiveness, warrant universal health coverage and improve outcomes. The paper shows some of the most relevant results emerged for the prediction of the most popular neurodegenerative diseases, and in particular a pipeline implemented for brain age prediction, exploiting deep learning. Some strategies to exploit these results are analyzed in order to create value for the society and the population, through a new service of Healthcare 4.0 based on the prediction of the most important neurodegenerative diseases, such as Alzheimer and Parkinson diseases.

Keywords. Technology transfer, Healthcare 4.0, machine learning, neurodegenerative diseases

Introduction

The health sector is particularly interesting for artificial intelligence (AI) applications, given the ongoing digitalization of health data and the promise for an improved quality of health and prevention (WHO Focus Group on Artificial Intelligence for Health).

By 2050, one in four people in Europe and North America will be over the age of 65 – this means the health systems will have to deal with more patients with complex needs. The management of these patients is expensive and requires systems to “shift from an episodic care-based philosophy to one that is much more proactive and focused on long-term care management” (Transforming healthcare with AI, 2020).

Artificial intelligence has the potential to revolutionize healthcare and help address some of these challenges, above all those related to neurodegenerative diseases which nowadays represent the challenge for Healthy and Active Ageing.

AI and machine learning will be the catalyst for transformation of health systems to improve efficiency and effectiveness, warrant universal health coverage (UHC) and impro-

ve outcomes (Panch, Szolovits et al., 2018).

The COVID 19 pandemic has highlighted the pressing need for improved data collection and exchange to better monitor and manage public health issues and health systems (Health at a Glance: Europe 2020).

With the creation of the European Health Data Space (EU 2020), the European Commission is currently developing a governance framework to promote a better use of health data, as well as a digital health infrastructure supporting such access. It will allow better use of data for health care, research, innovation and more evidence-based health policy-making (Health at a Glance: Europe 2020).

Fundamental transformation of health systems is critical to overcome these challenges and to achieve universal health coverage by 2030. Machine learning, the most tangible manifestation of artificial intelligence – and the newest growth area in digital technology – could be the catalyst for such a transformation (Panch, Szolovits et al., 2018).

The paper is organized as follow: Section 1 shows the important results emerged for the prediction of the most popular neurodegenerative diseases, and in particular a pipeline implemented for brain age prediction, exploiting deep learning; Section 2 presents some attempts for the valorization of these research results and their transfer in order to create impact on society. The conclusion of the paper is summarized in Section 3.

1. Deep learning approaches for neurodegenerative diseases

Neurodegenerative diseases affect a vast portion of the aging population and, of course, as life expectancy increases, this percentage is going to continuously grow. The onset of a neurodegenerative disease is usually related to several supportive features, among them an anomalous aging of the brain is particularly suitable for the early diagnosis pathological conditions. In brief, studying the structure, the organization and the functionality of the brain across the lifespan yields quantitative markers which can accurately discriminate the normal aging process from a pathological one. For example, measuring the difference between the chronological age of a patient and the brain age (usually referred to as “brain gap”) (Franke, Gaser, 2018; Bellantuono et al, 2021), estimated on the basis of specific age-related features such as cortical atrophy, allows the early detection of neurodegenerative processes.

The number of features which can be extracted to characterize a brain is huge, this is especially true when considering Magnetic Resonance Imaging (MRI) which capture the brain anatomy in millions of three dimensional voxels; therefore, the use of machine learning and deep learning approaches has become a necessity, both for computational and modelling purposes. Besides, several studies have demonstrated how such approaches can accurately predict the early onset of neurodegenerative diseases (Ashburner, 2007; Erus, Battapady et al, 2015; Konukoglu, Glocker et al, 2013; Sabuncu, Van Leemput, 2012). More recently, specific studies have explored the adoption of graph theory to model the brain a lay the foundations for novel characterizations of the brain and the possibility to add graph-based features to the standard (anatomical-based) ones (Amoroso et al, 2018 a; Amoroso et al, 2018 b; Amoroso et al, 2018 c).

To manage the computational complexity of these strategies and fully exploit their informative content, the role of computer facilities has gained a paramount importance. A simple pipeline for the analysis of brain connectivity could require 24-48 hours of CPU time, therefore the investigation of a medical database which can include thousands of subjects would be just unfeasible using a laptop or even a workstation. On the contrary, the use of computer farms composed by thousands of CPU, the adoption (when possible) of parallel computing paradigms and, more recently, the technological development due to GPU processing, make these analyses affordable.

Finally, a not secondary aspect to mention is the possibility offered by learning algorithms to explain how the features used to feed the adopted models affect their accuracy. There is an increasing attention towards explainable machine learning, intended as an effort to make machine learning algorithms (in some cases considered and used as “black boxes” by physicians and clinical practitioners) more interpretable and easier to understand [Lombardi et al, 2020; Roscher et al, 2020; Binder et al, 2021]. This aspect is fundamental to deepen our understanding of pathological conditions and their etiology.

2. Transfer of research results

In order to generate an innovation process based on the concept of Value Based Healthcare and on the quadruple helix model, it is necessary that all of the following Entities work together: Regions; Large public and private hospitals, also organized in networks; Private Life Science companies; Academies, University and Research Centers. In particular, the “Academy” has a key role in developing and disseminating methods and tools to support implementation. The Universities can play as a catalyst and “super-partes” coordinator in the innovation process for Healthcare 4.0 (Harvard Business Review Italia, 2021).

Through Knowledge transfer or research results valorization the Universities promote the dissemination and use of new technologies developed at the research organizations in order to increase the impact of the research for all the stakeholders (Scanlan, 2018); in fact, the researchers could be able to design new solutions or discover new methodologies useful to mitigate long-lasting healthcare issues.

The pipeline implemented for neurodegenerative diseases using AI and deep learning approach, illustrated in the previous Section, could be valorized and transferred in order to become a tangible innovation for the society in terms of predicting neurodegenerative diseases. Thus, the research results could be exploited through a variety of complex channels including research conversion to IP and its patenting and licensing activity, collaborative research with private sector firms or contract research consulting with Public stakeholders, creation of academic start-ups or entrepreneurial entities, etc.

Similarly to what is done by the best universities in the world such as MIT, Stanford University, California Institute of Technology, Berkeley University, Oxford University, Harvard, Imperial College London etc, ... which use different ways and channels to enhance their research and create impact on the territory for the promotion of a positive and sustainable social impact, the authors, in collaboration with the Technology Transfer Office of their university, are planning the most fruitful strategy to exploit these results

in order to create value for the society and the population. In fact, these results could be transformed into a new service of Healthcare 4.0 based on the prediction of the most important neurodegenerative diseases, such as Alzheimer and Parkinson diseases.

3. Conclusion

In this paper some aspects related to Technology Transfer in Healthcare 4.0 are presented. In particular, according to the requested digitalization of health, the use of machine learning solutions for neurodegenerative disease prediction is analyzed in order to create benefits and impact on the society and the territory.

References

- Whitepaper for the ITU/WHO Focus Group on Artificial Intelligence for Health - https://www.itu.int/en/ITU-T/focusgroups/ai4h/Documents/FG-AI4H_Whitepaper.pdf
- EIT HEALTH (2020), Transforming healthcare with AI - The impact on the workforce and organisations - <https://thinktank.eithealth.eu/wp-content/uploads/2020/12/EIT-Health-and-McKinsey-%E2%80%93-Transforming-Healthcare-with-AI.pdf>
- Panch T., Szolovits P., Atun R. (2018), Artificial intelligence, machine learning and health systems, *J Glob Health* Vol. 8 No. 2, 020303
- OECD/European Union (2020), HEALTH AT A GLANCE: EUROPE 2020, https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-europe-2020_82129230-en
- Spazio europeo dei dati sanitari, https://ec.europa.eu/health/ehealth/dataspace_it
- Franke K., Gaser C. (2018), Ten years of BrainAGE as a neuroimaging bio-marker of brain aging: What insights have we gained? *Frontiers in neurology* 10, 789
- Bellantuono L. et al. (2021), Predicting brain age with complex networks: From adolescence to adulthood, *Neuroimage* 225: 117458
- Ashburner J. (2007), A fast diffeomorphic image registration algorithm, *Neuroimage* 38 (1), 95–113
- Erus G., Battapady H., Satterthwaite T.D., Hakonarson H., Gur R.E., Davatzikos C., Gur R.C. (2015), Imaging patterns of brain development and their relationship to cognition, *Cereb. Cortex* 25 (6), 1676–1684
- Konukoglu E., Glocker B., Zikic D., Criminisi A. (2013), Neighbourhood approximation using randomized forests, *Med. Image Anal.* 17 (7), 790–804
- Sabuncu M.R., Van Leemput K. (2012), The relevance voxel machine (RVoxM): a self-tuning Bayesian model for informative image-based prediction, *IEEE Trans. Med. Imaging* 31 (12), 2290–2306
- a. Amoroso N. et al. (2018), Complex networks reveal early MRI markers of Parkinson's disease, *Medical image analysis* 48: 12-24
- b. Amoroso N. et al. (2018), Deep learning reveals Alzheimer's disease onset in MCI subjects: results from an international challenge, *Journal of neuro-science methods* 302: 3-9

c. Amoroso N. et al. (2018), Multiplex networks for early diagnosis of Alzheimer's disease, *Frontiers in aging neuroscience* 10: 365

Lombardi A. et al. (2020), Association between Structural Connectivity and Generalized Cognitive Spectrum in Alzheimer's Disease, *Brain Sciences* 10.11: 879.

Roscher R. et al. (2020), Explainable machine learning for scientific insights and discoveries, *IEEE Access* 8: 42200-42216

Binder A. et al. (2021), Morphological and molecular breast cancer profiling through explainable machine learning, *Nature Machine Intelligence*: 1-12.

Harvard Business Review Italia (2021), White paper: Le sei priorità per implementare il Value Based Healthcare in Italia -- https://www.hbritalia.it/userUpload/Implementare_il_Value_Based_Healthcare_in_Italia.pdf

Scanlan J. (2018), A capability maturity framework for knowledge transfer, *Industry and Higher Education* Vol. 32(4) 235–244

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