DeepECG4U

IDENTIFICATION OF PATIENTS AT RISK OF TORSADE DE POINTES, A LIFE-THREATENING ARRHYTHMIA USING ECG AND DEEP LEARNING

Project key information

Project leader : Edi Prifti, UMMISCO, IRD, 32 av. Henri Varagnat, 93140 Bondy, France; edi.prifti@ird.fr
Project duration : 42 months; Starting date : March 2021
IRD budget : 332 K€; Total budget : 674 K€

Partner institutions

IRD / UMMISCO, Bondy, France; Sorbonne Université; Université d'Evry, INSERM, APHP, Vanderbilt University

Context

Some cardiovascular diseases (such as congenital long QT syndrome, cLQTS) or drug-induced long QT syndrome (diLQTS), can cause a particular form of ventricular arrhythmia called Torsade de Pointes (TdP). While often self-terminating, TdP can degenerate leading to death. There are three main forms of cLQTS: type 1, caused by mutations in cardiac channel genes leading to IKs current blockade; type 2, IKr blockade and type 3, INaL activation. On Electrocardiogram (ECG), QT is prolonged in all these latter conditions, but ECG waveforms carry specificities including T-wave morphology abnormalities specific of each type of cLQTS. Most drugs responsible for diLQTS and eventually TdP, can be identified by assessing any of these mechanisms on the ECG. Therefore, diLQTS and cLQTS type 2 carry similarities in their ECG footprints. Regulatory agencies require new drugs to undergo thorough QT studies. It is however established that limiting the ECG evaluation to QT measurements is poorly predictive of TdP. Prediction of TdP risk and the characterization of the molecular mechanisms involved is of major interest for patients suspected to carry cLQTS as it is for other patients receiving drugs that may cause TdP. This is also a major issue for the pharmaceutical industry when developing new drugs. Finally, most physicians prescribing these drugs are unable to correctly quantify QT or evaluate TdP risk and do are not able to immediately consult with expert cardiologists.

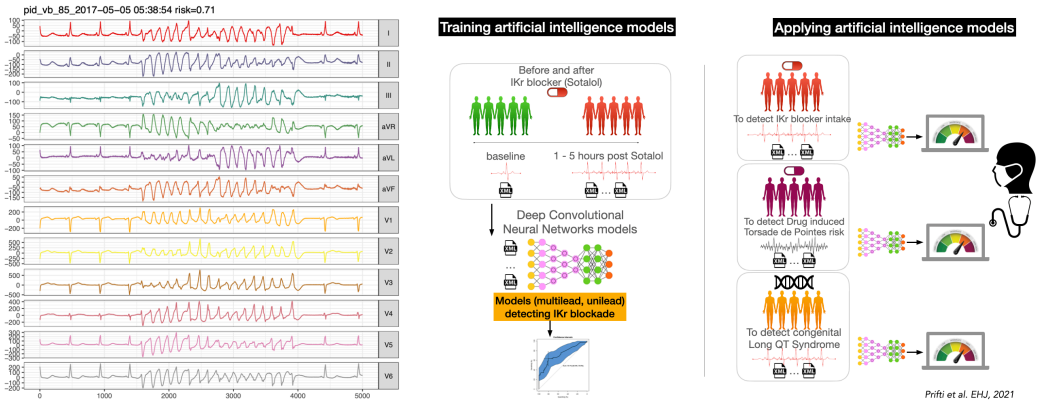

Figure 1: Left: An ECG illustrating a Torsade de Pointes event. Right: the experimental design used to train and test Convolutional Neural Networks in the objective of predicting TdP risk.

Objectives

Automatized personalized prediction for TdP risk of cLQTS or diLQTS patients, who may be unknown, can improve the accuracy of physician assessment and lower the risk of adverse events. In this project we aim to develop such a user-friendly tool using artificial intelligence, which is rapidly reaching medical practice. Deep learning (DL) in particular has brought a radical change in the field of pattern recognition and machine learning (ML) itself, improving most of the earlier models devoted to learning tasks such as image classification and natural language processing. Specifically, in cardiology, DL has recently been used for several applications, including the detection of various types of common arrhythmia such as atrial fibrillation, myocardial infarction, and cardiac contractile dysfunction. However, the use of DL in predicting TdP events in a drug-induced and congenital context has not yet been explored. In this project, we will use such algorithms that provide models that will not only increase precision but also provide clinicians with interpretable novel features and representations that could improve patient stratification. We expect that ECG annotation with the signal features that most influence the prediction would improve the understanding of the molecular mechanisms underlying TdP. Within the consortium, we have already explored the DL hypothesis and our preliminary results are very encouraging. The objective of our 3.5 year-long project is to advance this research topic, transform it into a translational application in several pilot cardiology departments during a first phase and design validation clinical trials during a second phase for widespread use in and out of hospital settings.

Organisation and expected results

This project involves 5 teams. IRD/Ummisco and Université d'Evry are experts in AI and Interpretability and Teams from INSERM, APHP, Sorbonne Université, and Vanderbilt University are world-class experts in cardiology (cLQTS, diLQTS and TdP). Moreover, they come with unique valuable datasets. The project will last 42 months. Key results will include (i) an integrated data repository (ii) DL models that predict TdP (iii) patient stratification and interpretability and (iv) a clinical application. The project is in full coherence with the government's objectives in accelerating AI-based translational applications in medicine and will most likely strengthen the position of France in the international arena.

Applications in the South

The IRD/Ummisco team is currently setting the collaborative framework in collaboration with researchers from UMMISCO/UCAD and cardiologists from Senegalese hospital to explore South specific cardiac diseases. The objective is to democratize the technologies developed in the deepECG4U project, where Moreover, several students from the International Doctoral Program are involved. The applications will consist of AI models coupled with portable ECG devices, which will be able to easily acquire ECG data.

References

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