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Another Godot who is still not coming: More on biomarkers for depression☆

Otro Godot que todavía no viene: más sobre los biomarcadores de depresión

Dear Editor,

The July 2021 Editorial inspired us to add another ''Godot'' to the list. As the Author pointed out[1] – *changing clinical guidelines in the traditionally biomarker-aversive field of psychiatry is not an easy step*-indeed. That so well applies to depression research, too.

The knowledge from decades-long research in complex systems dynamics offers tools for extracting information from electrophysiological signals (ECG, EEG, etc.). These tools provide high accuracy of detection of irregularities by quantifying subtle changes in signal patterns, using nonlinear measures, like different forms of statistical entropy (Shannon entropy, approximate entropy, sample entropy, multiscale entropy, etc.) or fractal dimension measures (Higuchi fractal dimension, detrended fluctuation analysis-DFA). Nonlinear parameters, like different forms of statistical entropy or fractal measures, calculated from electrophysiological signals (e.g., EEG or ECG), are demonstrated to be predictive of many psychiatric disorders and their phases. Beside diagnostics, complex system analysis can be used for monitoring therapy results (or forecasting responders to medication or other modalities of therapy like repetitive transcranial magnetic stimulation). Based on this analytic approach it is possible not only to accurately confirm depression, but also delineate between phases of disease (episode vs remission, like in[2]), differentiate between subtypes (melancholic vs non-melancholic depression), comorbidities, or even detect existing suicide risk.[3] Knowing those additional information early in the process can help in effectively choosing the therapy that increases the probability that the patient would recover and avoid relapses. Pincus[4] stresses the importance of *dynamics* of the systems, which requires a quantifier that is sensitive to the order of events in time series, for example, approximate entropy (ApEn). There is a lot of research demonstrating that nonlinear measures are much more accurate and reliable than the conventional ones in analyzing history sensitive systems.[5] Widely used Fourier transform that is embedded in any software in any operating machine made to record electrophysiological signals, is proven to be redundant to fractal analysis[6] and it is known to be not sensitive to detect early changes in the signal unlike other fractal and nonlinear methods.[7]

Perhaps especially urgent is detecting cardiovascular diseases (CVD) in people suffering from depression. The connection between these two diseases that carries a high mortality risk[8] has long been known[9] and yet monitoring heart function in depressive patients is far from clinical routine. The data can be easily obtained by novel portable ECG monitoring devices that are approved as medical-grade signal quality equivalent to holter, but are much more practical and comfortable to use by the patient her-/himself, leading to early detection of risks and potentially to personalized medicine at its very best. The data can then be processed by a combination of nonlinear analytics and advanced statistical procedures (to control, for example, for comorbidities, subtypes and other confounding factors[10]). Even better, the analysis can be empowered with machine learning applications[11] that are widely in use due to high power of computation and cloud computing.

This process is neither costly nor invasive, so, why wait to save lives?

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Discontinuation of maintenance electroconvulsive therapy: Lessons learned from the COVID-19 pandemic

Discontinuación de la terapia electroconvulsiva de mantenimiento: lecciones aprendidas de la pandemia COVID-19

Dear Editor,

The COVID-19 pandemic has raised serious concerns in all healthcare systems. Due to this exceptional situation, many aspects of regular medical practice have had to be reconsidered. Unfortunately, ECT and other medical services, labeled as ''non-urgent'' or ''non-essential'' and have been delayed.[1,2] Maintenance ECT (M-ECT) has been particularly affected: the time between treatments has been prolonged[1] or fully discontinued in many hospitals.[3–7] Literature on the outcome of patients discontinuing M-ECT is limited, but the data suggest high rates of relapse (44–50%), especially in the first year after discontinuation.[8,9]

In our hospital, ECT was halted completely on March 18, 2020, mainly due to the reassignment of anesthesiologists to the intensive care units. Normal activity was not resumed until May 8, 2020. At the time of cessation of ECT, 37 patients were on the ECT program, 33 of them receiving M-ECT. Our real-world prospective study aims to characterize the clinical outcome of these patients, from the time of the interruption of M-ECT until January 15, 2021, and to analyze the related cost–benefit ratio. Demographic, clinical and M-ECT data were recorded. A relapse was defined as the need for hospital admission, or the need for a new acute ECT course; M-ECT was also reestablished in the case of early signs of relapse. The study was approved by the Hospital Ethics Committee.

Descriptive and survival analysis were performed (a Kaplan–Meier to estimate the time until full clinical relapse or the occurrence of early signs of decompensation, and a univariate Cox analysis to identify potentially contributing factors). Variables that displayed significant associations were entered into a multivariate Cox regression model. A cost estimate was made, determining the economic ''savings'' in M-ECT sessions during the period in which ECT was not applied, the ''saved sessions'' in patients who to date have not restarted M-ECT as well as the cost in days of admission and the number of additional ECT sessions.

Nineteen of the 33 patients (57.6%) were female (with a mean age of 67.12 years (±12.1; 40–85)). Sixteen patients (48.5%) met criteria for major depressive disorder. The mean number of previous episodes in the last five years was 3.52 (±3.2). The mean duration of M-ECT was 41.78 months (±52.4; 1.45–273.1). Twenty-six patients (78.8%) were receiving M-ECT at a monthly frequency or higher at the time of treatment discontinuation. One of the patients on the M-ECT program died of COVID-19 in March 2020.

When the ECT program was resumed a risk-benefit analysis was made, prioritizing acute ECT. Regarding the clinical course of the 32 patients, 19 (59.4%) met criteria for relapse (eight patients (25%) need for hospital admission or a new acute ECT course) or experienced early signs of relapse and M-ECT was reestablished (11 patients, 34.4%). The mean time to relapse or the emergence of early signs of relapse was 88.84 days (±78.8; 61 median, 15–290). Furthermore, two patients preferred to restart M-ECT despite having no relapse symptoms. Finally, to date, 11 patients (34.4%) have opted not to restart M-ECT while awaiting the evolution of the pandemic, and are clinically stable. As of January 15, 2021, 62.5% of patients (20/32) had resumed M-ECT.