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RESEARCH ARTICLE

Geolocated Wireless Heart Rate Variability Sentinel Surveillance in Immunological Assessment, Intervention and Research Concerning COVID-19 and other Pandemic Threats

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ABSTRACT

With the development of increasingly sophisticated biotechnology and conceptual/analytic approaches, a greater ability to understand, intervene and prevent disease and promote health is becoming more available. A synthetic integration of several such technologies and analytic strategies named the Canary System is described which can impact significant global health problems, including the COVID-19 pandemic with its continuously evolving variants. The system wirelessly acquires high fidelity heart rate variability and other data, geocodes the data and transfers it through personal device for high throughput algorithmic analysis, which has been shown to indicate likely COVID-19 status well before clinical symptoms emerge, if indeed the individual becomes symptomatic. The system can not only provide sentinel surveillance and other public health activities, but can facilitate research in disciplines such as immunology, virology, epidemiology, affective and cognitive neurobiology and health psychology. The aim and scope of this paper is to, within context, describe both the rationale and functional components and operation of this system in a variety of settings. The objective of the paper is to explicate both the operational characteristics of this approach and the multiple applications it may have in the disciplines identified above as well as primary health care and non-medical applications.

Introduction:

The development of new measurement or observation techniques frequently facilitates scientific progress, as illustrated by the microscope and telescope, among many other increasingly sophisticated innovations. Studying complex systems such as the immune system (IS), both at 1) the microscopic level of genetic and microbiomic phenomena, and 2) the analytic and synthetic power of Big Data algorithms and artificial intelligence, has brought about significant progress in our understanding and ability to intervene effectively and safely. Evolutionary biology¹ suggests that the IS has both innate and adaptive aspects and that the adaptive aspects can function as an additional evolutionary mechanism beyond strictly genetic evolution. This is a much more rapid phenomena than genetic evolution through natural selection and is a type of learning which may be harnessed to increase the adaptive fitness of organisms, groups, and cultures. Such enhanced adaptive fitness can aid the IS in its functioning as a defender of health and functional capability against a wide variety of pathogens and other environmental challenges. The overarching conceptual framework adopted here is complex adaptive systems which emphasizes the emergence of complex adaptive outcomes resulting from the interaction of multiple constituent agents frequently through processes of self-organization consistent with organic life, rather than top-down command and control planning².

Recently, the use of digital technology has allowed investigators to observe and intervene in much broader and more precise ways than previously possible. The collection of continuous longitudinal vital psychobiological data from intact humans in their natural environments has furnished high fidelity, inexpensive and scalable data on many variables important to IS and related fields such as epidemiology, virology and especially public health. Heart rate variability (HRV) is one such variable that has demonstrated contributions to the understanding, intervention, and prevention of disease³ as well as providing early warning of developing pathogens and pathological conditions via sentinel surveillance⁴. The importance of this development is in the context of Global Health, especially its immunological aspects.

Global Health encompasses the broadest application of immunology, virology, epidemiology and public health policy⁵⁻⁸. It is well established that the major improvements in overall population health status have historically derived from

epidemiological findings and public health intervention, especially sanitation and water treatment, rather than clinical medicine. This was the beginning of Non-Medical Interventions (NMI). While developments such as vaccination and antibiotics and other pharmacological agents have been extremely important, innovation such as development of the randomized clinical trial and institutions such as the FDA have been instrumental in realizing and reinforcing these improvements and assuring that proposed interventions are both safe and effective. Notably, before public outcry forced the development of the FDA, most putative medical products ("snake oil" patent medicines) were generally ineffective beyond placebo effects and some were quite dangerous, including both toxicity and addictive properties. The maximum benefit occurs when both clinical medicine and public health interventions are combined in an equitable fashion for populations. As the phenomenon of globalization has proceeded, the connectedness of humans has been increased through modern transportation and communication, making the development of pandemics more likely. It has been shown that significant health disparities exist globally, especially in countries without functional universal healthcare systems, such as the United States. There are also strong cultural and social factors which have hindered the development and dissemination of valuable knowledge. Galileo was threatened with death for proposing his heliocentric theory of our solar system, while Darwin was merely ignored, ridiculed, and threatened for his evolutionary theories. Semmelweis was ejected from the Vienna Medical Society for his observation that maternal and child morbidity and mortality decreased when sanitary procedures were followed during childbirth, even though germ theory was yet to be widely accepted. The phrase "Enemy of the People" was not coined by former President of the US Donald Trump or other politicians such as Stalin and Khrushchev but by Norwegian playwright Henrik Ibsen who described the fictional Dr. Thomas Stockmann, the town doctor who discovered that the spa which provided the main economic sustenance for the town was polluted. When he refused to suppress his findings, virtually the entire town attacked him and his family and the town government removed him from his job and home. Notably, in the current COVID-19 pandemic, President Trump referred to Dr. Anthony Fauci and other public health and medical researchers as "enemies" when they expressed opinions about the

pandemic which the President found threatening to his self-image as a “genius”.

Other psychological and behavioral phenomena are also present which hinder effective public health intervention. Initially the US President refused to recognize the COVID-19 infections and stated they would “disappear”. Aided by disinformation in social and conventional media, significant numbers of people refused to adhere to proven public health NMI regarding social distancing and mask use, claiming such practices infringed on their freedom. Similarly, “anti-vaxxers” either stated that vaccination was harmful or unnecessary. Such actions, especially by visible government officials and celebrities, not to mention “influencers”, made an already difficult situation more unstable and led to mortality in the US in excess of one million lives and six million globally. Thus, effective public health measures must take cognizance of such destructive factors and develop effective countermeasures, based on sound public education and information policies. As Wilson has stated “policy is a branch of biology”¹ and other sciences. Another aspect of effective public health policy is sentinel surveillance. Especially in developing pandemics, it is often too late to wait for trailing indicators such as mortality data, and systematic surveillance of sentinel populations of both humans and animals can identify pathogens of concern and emerging disease before they spread out of control. In the case of the COVID-19 pandemic, for example, physiological observations of humans such as increased temperature, decreased blood oxygen saturation, decreased activity level and suppressed heart rate variability are leading indicators that occur days before subjective symptoms lead to doctor visits. Also, observations of samples of suspect animals such as the thirty billion chickens raised for meat consumption worldwide can identify zoonotic transmission, giving critical lead time in identifying and managing outbreaks. Another measure, although indirect, is wastewater treatment plant process analysis. A final note of effective policy is the development through the WHO and other institutions of a Global Pandemic Treaty which establishes enforceable protocols for signatories to handle potential emerging pandemics or other health crises in a unified transparent and cooperative manner This could be coordinated by Johns Hopkin’s proposed Center for Epidemic Forecasting⁹.

Methods

For the purposes of this paper, the most salient single variable that can be used in such a manner is heart rate variability (HRV). HRV is a measure of the instantaneous change in variability that accompanies each successive heartbeat (interbeat interval) and has been studied extensively as not only a sensitive predictor of all-cause mortality, but an indicator of many physical diseases conditions, including immunological disease and psychosocial functioning as well³. A current search of the terms “heart rate variability” and “HRV” in PubMed reveals over eleven thousand references. The seminal contributions of Porges’ Polyvagal Theory¹⁰ and Thayer’s Neurovisceral Integration Theory¹¹ are notable. Drury et al³ present an extensive review of applications of HRV in various clinical and other performance situations. How HRV can be used in COVID-19 detection is described in Drury et al⁴ and will be explored in greater detail below.

The acquisition of physiological data has been enhanced dramatically by the development of personal health devices which can measure heart rate, temperature, blood oxygen saturation, activity level, GPS location and various other parameters with acceptable reliability and validity. This practice is also termed remote patient monitoring in medical settings, and especially valuable in epidemiological application where GPS geolocation data can help identify clusters of cases or pathogens of concern. While the quality of these devices varies dramatically, some are able to collect laboratory grade data. Additionally, using Bluetooth and other file transfer protocols, these data are able to be transferred to personal device such as cell phones and then sent for analyses by remote servers. A commercial concern, Kinsa, has demonstrated that their Bluetooth thermometer can acquire and record temperature data. While there have been misadventures and high-profile failures, effective use of such a system to acquire transfer and analyze HRV data by algorithm has been described⁴. While this application represents the current state of existing useable off the shelf technology, research is advancing rapidly and the feasibility of implanting such sensors is being explored, with appropriate protections for privacy and data security. The use of materials such as graphene is also rapidly expanding and may improve data acquisition. Since recharging batteries is a major compliance issue in personal fitness devices, wireless capacitance charging and even use of the body’s own biochemistry to power

the sensor system is theoretically possible. The use of soft penetrating electrodes has been demonstrated and allows for more accurate data collection.

The detailed aspects of this approach are described by Jarczok et al¹² who studied 9550 adults. Individual beat to beat heart rate data which can be wirelessly acquired through devices such as the Oura ring, are processed through an algorithm which extracts root mean square of successive differences (RMSSD), a frequently used HRV metric. Both daytime and nighttime RMSSD values indicate elevated risk and allow for the development of the Canary System

Results:

The key to practical and effective assessment and intervention systems is the ability to communicate with high quality data transmission between system elements. Thus far, we have presented data that show high quality data acquisition of relevant health and well being parameters is possible. Our study of using wireless HRV data in detecting COVID symptoms remotely⁴ is proof of concept but is only the beginning of the possible uses of machine learning and other Big Data approaches. With data that may have predominantly non-linear characteristics, appropriate analytic strategies are necessary and AI approaches such as reinforcement deep learning have shown promise. Also, multivariate data analysis can be improved by machine learning techniques. An intriguing application of multi agent networking is the use of psychophysiological data to integrate the effective functioning of high-performance teams such as the Naval Sea Warfare SEALS special operators. These teams often function in settings where verbal communication is limited and dangerous, yet knowledge of each members functional status is critical. Topol¹³ has cautiously described Deep Medicine as an approach to using such AI approaches to improve medical outcomes. The progress noted by Johnson's Extra Life¹⁴ shows that many items in the "catalog of evils" have been deleted, many by innovative data analytic or visualization schemes starting with Farr's mortality tables and Snow's mapping of the Broad Street pump morbidity/mortality., as well as innovative concepts (such as the randomized controlled trial) and institutions (such as the Federal Drug Administration). The use of networked sensors can also facilitate immunological studies by demonstrating adaptive immune function in vivo and continuously.

Discussion and Conclusion:

It is apparent that the development of advanced algorithmic data analytic techniques combined with increasingly sophisticated physiological data acquisition technologies has brought about significant benefits for human health and well-being, but this work is just beginning. The review of the history of public and clinical health above shows multiple examples of inflection points that have improved our health yet left many still suffering. Despite the existence of both the WHO and CDC, for example, no single data repository on the all global COVID-19 cases existed and had to be cobbled together by an ad hoc group of academics and researchers had to fill this void. This group highlighted the crucial role of NMs such as masking, ventilation, and social distancing in managing pandemic development. But the key aspect of the present paper is to use multiple agents, human, technical and computational, to bring about progress in human health. Beyond taking advantage of the massive amounts of physiological/immunological, psychological, and behavioral data becoming increasingly available, technological developments such as Google's Deep Mind explorations by Alpha Zero and now MuZero¹⁵ can contribute computational agents in this synthetic complex. The use of wireless geolocated sensors throughput to advanced reinforcement and machine learning techniques and other artificial intelligence applications is offered as a currently available methodology for sentinel surveillance of COVID-19 outbreaks and other viral and bacterial threats. This will not only facilitate global public health but facilitate more sophisticated research in areas such as immunology, virology, and epidemiology.

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