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Published in:
Big Data and Society

DOI:
10.1177/20539517221145680

2023

Document Version:
Publisher's PDF, also known as Version of record

Original Research Article

BIG DATA & SOCIETY

Big Data & Society
January–June: 1–13

DOI: 10.1177/20539517221145680
journals.sagepub.com/home/bds
SAGE

Short-circuiting biology: Digital phenotypes, digital biomarkers, and shifting gazes in psychiatry

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Abstract

Digital phenotyping is a rapidly growing research field promising to transform how psychiatry measures, classifies, predicts, and explains human behavior. This article advances the social-scientific examination of digital phenotyping's epistemology and knowledge claims. Drawing on the notion of a "neuromolecular gaze" in psychiatry since the 1960s, it suggests that digital phenotyping concerns a new psychiatric gaze—the "digital gaze." Rather than privileging neuromolecular explanations, the digital gaze privileges the "deep" physiological, behavioral, and social "truths" afforded by digital technologies and big data. The article interrogates two concepts directing the digital gaze: "digital phenotype" and "digital biomarkers." Both concepts make explicit an epistemic link between "the digital" and "the biological." The article examines the soundness and construction of this link to, first, offer a "reality check" of digital phenotyping's claims and, second, more clearly delineate and demarcate the digital gaze. It argues there is evidence of significant mis- and overstatements about digital phenotyping's basis in biology, including in much-hyped psychiatric digital biomarker research. Rather than driving the biologization of digital traces, as some have suggested, digital mental health phenotyping so far seems mainly concerned with physiological, behavioral, and social processes that can be surveilled by means of digital devices.

Keywords

Digital phenotyping, digital biomarker, digital gaze, psychiatry, neuroscience, surveillance

Introduction

In recent years, researchers in various disciplines (e.g. psychiatry, data science, psychology, sociology, philosophy, and ethics) have claimed that the introduction of digital technologies such as smartphones, together with big data analytics such as machine learning, is causing profound epistemic changes in psychiatry (e.g. Engelmann, 2022; Insel, 2017; Marsch, 2021). If epistemic changes are indeed occurring, as many suggest, they are important to analyze not least because of the impacts psychiatric technologies and knowledge have on individuals and society. Psychiatric technologies and knowledge—often mediated through psychiatric expertise (Rose, 2018)—help "make up people" through the power of classification and intervention (Hacking, 1986), fostering logics and practices of surveillance and governance by installing ways of understanding and acting upon ourselves and others (Rose, 2006), and creating and sustaining political economies by opening up pathways towards psychiatric innovation and commercialization (Healy, 2003). Perhaps the prime example of this is how the rise of psychopharmacology since the mid-1950s (Healy, 2009) contributed to new ways of studying and classifying mental illness through the lens of drugs (Moncrieff, 2008); new ways of governing and treating people with drugs inside and outside psychiatric institutions (Shorter, 1997); and the growing association between drug companies, psychopharmacological researchers, and the psychiatric profession (Healy, 2003).

Rose and Abi-Rached (2013) have characterized the epistemic changes that psychopharmacology helped bring about as the birth of a "neuromolecular gaze." The notion of a neuromolecular gaze takes inspiration from Michel Foucault's (1973) notion of shifting medical gazes and from Ludwik Fleck's (1979) theory of styles of thought as "the entirety of intellectual preparedness for one particular way of seeing or acting, but not for another" among scientific "thought collectives" (p. 64). In the 1960s, Rose and Abi-Rached (2013) argued, a neuromolecular gaze directed

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psychiatric research and practice toward the chemical and biological intricacies of the brain. Its birthplace was a thought collective spanning academia, industry, and government that saw the molecular level as *necessary*—and perhaps even sufficient—for unraveling the causes of mental illnesses, and for their effective diagnosis, management, and resolution. Over the ensuing decades, the neuromolecular gaze came to dominate psychiatry and replace the focus on the human mind or psyche, which had captured the imagination of an earlier generation of psychiatrists (Rose, 1998).

As a corollary, it was (and, arguably, still is) expected that psychiatry and allied sciences should be able to identify these molecular anomalies in the brain, or at least uncover biological markers of brain disorders—the sought-after *biomarkers*—that would ensure the accurate diagnosis and prognosis of mental pathologies. Furthermore, once these molecular abnormalities have been identified, drug companies should be able to design more effective therapies by targeting the molecular bases of specific brain disorders (Singh and Rose, 2009). In 2003, Steven Hyman, Director of the US National Institute of Mental Health (NIMH), 1996–2001, remained confident about this neuroscientific research agenda when writing for *Scientific American*:

> By combining neuroimaging with genetic studies, physicians may eventually be able to move psychiatric diagnoses out of the realm of symptom checklists and into the domain of objective medical tests. Genetic testing of patients could reveal who is at high risk of developing a disorder such as schizophrenia or depression. Doctors could then use the neuroimaging on the high-risk patients to determine whether the disorder has actually set in. I do not want to sound too optimistic—the task is daunting. But the current pace of technological development augurs well for progress. (Hyman, 2003: 103)

However, for over a decade now, there have been recurring claims that the neuroscientific agenda has exhausted itself. Top-ranking researchers (Agid et al., 2007) and pharmaceutical executives (Miller, 2010) have openly pondered the causes of and solutions to the lack of progress in diagnosing, explaining, and treating mental illness. As evidence of this perceived crisis, many leading drug companies have reduced or shuttered in-house neuroscientific research, despite the massive scale of the psychotropic drug market. Perhaps the most widely broadcast statement of this crisis came from Thomas Insel—Hyman's successor as NIMH Director, a position Insel held until 2015—who in 2017 told a journalist from *Wired*:

> I spent 13 years at NIMH really pushing on the neuroscience and genetics of mental disorders, and when I look back on that I realize that while I think I succeeded at getting lots of really cool papers published by cool scientists at fairly large costs—I think $20 billion—I don't think we moved the needle in reducing suicide, reducing hospitalizations, improving recovery for the tens of millions of people who have mental illness … I hold myself accountable for that. (Rogers, 2017)

Yet, Insel has also taken it upon himself to become a spokesperson for what he, and many others, see as the solution to psychiatry's impasse: *digital technologies combined with big data analytics* (Insel, 2017). In psychiatry, as in other areas of medicine, "the digital" and "big data" have become a new repository of hope and anticipation (Lupton, 2017; Pickersgill, 2019). In particular, the last decade has seen the emergence of a self-identified "digital phenotyping movement" (Baumeister and Montag, 2019: xviii) seeking a novel approach to mental health by using digitally collected data to assess individuals' mental health phenotypes. Specifically, digital phenotyping promises to harvest and analyze vast volumes of digital data said to capture a person's everyday physical and social dynamics, cognitive states and traits, and attitudes and emotions. These data can be collected continuously, for example, as smartphone GPS, sensor, keyboard, social media, voice, and speech data, and used to compute predictive mental health models and risk assessments, ultimately for designing behavioral nudges and treatments.

For its champions, digital phenotyping has revolutionary implications (Baumeister and Montag, 2019; Insel, 2017; Jain et al., 2015; Torous et al., 2017). Digital phenotyping not only proposes a digital solution for mental health surveillance and management, but is imagined as rewriting the atlas of psychiatric research and practice by transforming how psychiatry measures, classifies, predicts, and explains human behavior (Engelmann, 2022). Digital phenotyping appears to herald a new psychiatric gaze—what I call a *digital gaze*. This gaze seeks truth neither in the microscopic neuromolecular processes measured in clinical or experimental settings (Rose and Abi-Rached, 2013) nor in psychological or statistical assessments of persons' self-reported or overt deviant behavior (Rose, 1998). Rather, in this new gaze, the truth lies in the *deep profiling* of people's everyday life using *digitized big data* conceived as ubiquitous (as opposed to sporadic), proximal (as opposed to distant), continuous (as opposed to intermittent), and objective (as opposed to subjective).

This article seeks to advance the burgeoning social scientific research on this apparent shift in psychiatric epistemology by engaging critically with this digital gaze. More precisely, following calls for engagement with the empirical claims, language, imaginaries, and metaphors employed by digital phenotypers (Birk and Samuel, 2020; Engelmann, 2022), and informed by previous critical engagements with psychiatry (Rose, 2018) and the neurosciences (Choudhury and Slaby, 2016), I interrogate two central concepts directing the digital gaze: the "digital phenotype" and

"digital biomarkers." Both concepts make explicit an epistemic link between "the digital" and "the biological." What I suggest is that this epistemic link is *much weaker* than commonly recognized. Indeed, initially establishing the link has involved misappropriating a biological concept (i.e. the "extended phenotype" imported from evolutionary biology) and stretching another beyond recognition (i.e. "biomarkers" imported from molecular medicine). Montag et al. (2021a), key experts in the field, have foregrounded this issue by asking their research community: "How much biology needs to be in a digital biomarker?" To this, my answer is: currently very little to none.

By highlighting this, I seek, first, to offer a "reality check" of psychiatric research proposed by Choudhury and Slaby (2016), intended to deepen debate and reflection concerning the field. Such reality checks interrogate both the soundness and construction of scientific claims and frameworks (Rose, 2011), helping advance interdisciplinary discussions about psychiatric research broadly (Choudhury and Slaby, 2016), as well as about specific research, for example, neurochemical theories of mental illness (Moncrieff, 2008) and brain imaging studies (Dumit, 2011). Here, I suggest that a reality check of digital phenotyping's use of two biological concepts challenges the notion that digital phenotyping is driving the biologization of digital traces and, therefore, that digital phenotyping risks the further biologization of psychiatry warned by some social scientists (e.g. Baumgartner, 2021; Birk and Samuel, 2020).

The second aim is to underscore the connections of digital phenotyping's gaze beyond biology and even medicine, but that may be concealed or downplayed by recurrent (yet nebulous) references to "bio." Particularly, as the next section argues, what risks being downplayed are the connections that the digital gaze has to the broader sociohistorical and commercial trend of using digital data for individual surveillance and behavioral manipulation (Zuboff, 2015), and to the general rise of a big data gaze in the social and behavioral sciences (Kitchin, 2014).

Defining the contours of a new psychiatric gaze

Equipped with sensibility concerning the power of psychiatric technologies and expertise, a growing number of social scientists have tried to make sense of the emerging digital phenotyping movement and its epistemology (e.g. Baumgartner, 2021; Birk et al., 2021; Birk and Samuel, 2020; Coghlan and D'Alfonso, 2021; Cosgrove et al., 2020a; Engelmann, 2022; Rowe, 2021; Stark, 2018). Admittedly, the social scientific analysis is—like the field of digital phenotyping itself—in an early phase, but still, several important topics have been covered. Below, I discuss three interrelated topics that address the question of shifting gazes in psychiatry.

Digital phenotyping's socioeconomic relations

First, several scholars note how digital phenotyping's vision of ubiquitous digital surveillance for mental health cannot be separated from the socio-historical trend towards intensified government and commercial digital surveillance and behavioral control (Cosgrove et al., 2020b; Engelmann, 2022; Rowe, 2021; Stark, 2018). This does not imply that digital phenotyping is the simple reflection of a "surveillance state" (Mitchell and Diamond, 2018) and/or "surveillance capitalism" (Zuboff, 2015). However, what is clear from previous research is the existence of financial, technological, and ideological ties between the digital phenotyping thought collective and the government and commercial engines of everyday digital surveillance (Prainsack, 2020). This could be analogous to the ties between psychiatric pharmacologists, government agencies, and the pharmaceutical industry, which have been a defining feature of the psychopharmacological era (Healy, 2009).

Illustrating this is Tomas Insel's resignation as NIMH Director in 2015 to lead Google's mental health team focused on digital phenotyping (Carey, 2015). Admittedly, Insel has sought to distance digital phenotyping, which, he says, uses digital technology "in a medical setting where consenting patients and families can be empowered with information" from "the appearance of and very real risk of surveillance" associated with the use of the same technology for large-scale behavioral or cognitive monitoring, which "can be a first step towards the slippery slope towards surveillance" (Insel, 2019: vii–viii). Yet, as Stark (2018) has noted, big tech companies and platforms, such as Facebook, have experimented with digital phenotyping and mood modification for years using increasingly powerful tools for digital surveillance and behavioral control (e.g. Kramer et al., 2014; see also Rowe, 2021). Sociologists Golder and Macy's (2014) enthusiastic depiction of the promises of online social research, an allied field of inquiry, makes this point clear:

> What is new is the macroscopic global scale and microscopic behavioral extensiveness of the data that are becoming available for social and behavioral science. The web sees everything and forgets nothing. Each click and key press resides in a data warehouse waiting to be mined for insights into behavior, to enable useful functions from spam detection to product recommendations to targeted advertising. Our mobile phones, tablets, and laptops report every web page we visit and every link we click and can even report our precise location and movements. Our social interactions are mediated through email, Skype, instant messaging, Facebook, and Twitter. Our photographs are identity-tagged, geo-tagged, and time-stamped, creating a who-when-and-where recording of everything we upload. Social media platforms like

> Facebook and online labor markets like Amazon Mechanical Turk enable controlled experiments using thousands of participants from all over the world. (pp. 131–132)

Importantly, similar enthusiastic visions of the epistemic revolution enabled by the ubiquitous digital recordings of everyday life are found in the programmatic declarations of digital phenotypers. For example, Baumeister and Montag (2019: xv) offered the following view of how the new "digital image of our lives" can provide "the data basis necessary to estimate people's traits, states, attitudes, cognitions, and emotions." They write:

> What does your smartphone usage pattern tell us about you and your state of mind? What does your vacation, social, and work life pictures posted in social networks tell us about your happiness and your attitude toward work, holiday time, and your spouse? Would we recognize a change in mental state when comparing voice recordings from today and 5 years ago? What will your lunch look like tomorrow? You might not know it, but maybe your biosensing signals will tell us now already. Two advances enable us to provide increasingly sophisticated digital phenotyping estimates: Big Data and machine/deep learning approaches. (Baumeister and Montag, 2019: xv)

Significantly, this is a vision of "a digital, all-seeing, all-digesting epidemiology" (Engelmann, 2022: 8) that rests, effectively, on a technological and commercial apparatus of everyday surveillance that is simultaneously massive and microscopic in scale (Prainsack, 2020).

Digital phenotyping's academic relations

The above two quotations lead to the second topic, concerning the question of potential epistemic change: the origins of digital phenotyping as a *research program* and its relations to various academic trends and disciplines. As a multidisciplinary and technologically sophisticated approach to behavior, digital phenotyping unsurprisingly has multiple academic origins and relations, much as the neurosciences originated as "hybrid of hybrids" in academia (Rose and Abi-Rached, 2013). Indeed, Engelmann (2022) noted that digital phenotyping has multiple origins in the context of the proliferation of big data in medicine. One origin is within precision or personalized medicine's search for biomarkers of disease. Specifically, for both Engelmann (2022) and Baumgartner (2021), digital phenotyping exploits, and seeks to address, psychiatry's failure in linking diseases (phenotypes) to genetics (genotypes). Rather than focusing on the genotype side of the equation, as much molecular psychiatry and psychiatric genetics does, it proposes—again quoting Insel (2017: 1216)—"a fresh look at behavior, cognition, and mood" using huge amounts of digital data.

Broadly, this faith in the large-scale quantification of phenotypic data for solving genotype–phenotype riddles is aligned with Houle et al.'s (2010) influential article advocating a *phenomics* approach in biology, comparable to the genomics approach, to better understand the pathways connecting genotypes to phenotypes: "The question 'why not measure it all?' was fortunately affirmatively answered for genomes; it is now time to ask the same question for phenotypes" (p. 855). In the context of precision medicine, the programmatic idea of high-throughput quantification of phenotypic data ("why not measure it all?") is increasingly branded as "deep phenotyping," of which digital phenotyping is often portrayed as a sub-field (Torous et al., 2016). At first sight, deep phenotyping—and hence digital phenotyping—echoes the notion and technologies of *deep* DNA or RNA sequencing, or deep genotyping, that revolutionized the field of genomics by allowing multiple reads of the same genomic sequences, sometimes hundreds or thousands of times (the technical definition of sequencing depth), increasing sequencing accuracy and permitting the assessment of heterogeneous genetic samples (Simz et al., 2014). Indeed, explicit parallels between deep genotyping and deep phenotyping abound (e.g. Bycroft et al., 2018). However, Engelmann (2022) has suggested that the notion of "depth" in digital phenotyping is ambiguous and increasingly connected with the metaphors and language of artificial intelligence (e.g. DeepMind, DeepBlue, DeepFace, and DeepMood), where digital phenotyping is supposed to "provide causal depth" to illness phenotypes by going beyond the surface of "shallow" medicine by using techniques such as deep learning.

Stark (2018: 216), in contrast, placed the emergence of digital phenotyping not within the biological or biomedical sciences' recent interests in the high-throughput quantification of phenotypes or in artificial intelligence, but "within a long-intertwined history of psychology and computing," leading up to the emotional surveillance and behavioral tracking conducted by companies such as Facebook, which he calls *algorithmic psychometrics*. Indeed, in many ways, digital phenotyping appears to have more in common with computational social science approaches to behavior (Kitchin, 2014) than with neuroscientific or genetic approaches to illness (Rose and Abi-Rached, 2013). Testifying to this academic relation, the edited volume *Digital Phenotyping and Mobile Sensing* has the illustrative subtitle *New Developments in Psychoinformatics* (Baumeister and Montag, 2019). Significantly, the volume contains many examples of digital phenotyping from outside the type of medical setting that Insel, in the foreword to the volume, said can protect against "the appearance of and very real risk of surveillance" (Insel, 2019: vii), including from the growing area of "predictive education analytics" (Williamson, 2016). For example, Cao et al. (2019) described surveilling the behavioral patterns of almost 20,000 Chinese undergraduate students using digital data obtained from students' campus smart cards used both to

open/close doors and as a payment medium. In total, there were:

> … 3,151,783 records for taking showers in dormitories, 19,015,773 records for having meals in cafeterias, 3,412,587 records for entering/exiting the library and 2,279,592 records for fetching water in teaching buildings, respectively. In addition, some other consumption and entry–exit behaviors are also recorded, including purchasing daily necessities in campus supermarkets, doing the laundry, having coffees in cafes, taking school buses, entering/exiting the dormitories and so on. GPAs of undergraduate students in each semester are also collected. (Cao et al., 2018: 6)

According to Cao et al. (2019), their work illustrated how orderliness (based on taking showers and having meals) and diligence (based on entering/exiting the library and fetching water in teaching buildings) predicts academic performance—a finding that "helps education administrators quantitatively understand the major behavioral factors that affect academic performance and provides a promising methodology towards quantitative and personalized education management" (Cao et al., 2018: 2).

Significantly, these two disciplinary relations—precision medicine and algorithmic psychometrics—are reflected in Dagnum and Montag's (2019) assertion that digital phenotyping can be seen as encompassing two distinct areas of inquiry: *digital biomarkers* and *behavioral phenotyping*. While the search for digital biomarkers is more narrowly concerned with identifying informative digital correlates of disease, behavioral phenotyping takes a broader perspective on the digital phenotype in order to contribute to the psychosocial sciences (e.g. Mohr et al., 2017)—something leading digital phenotypers have framed as a logical extension of evolutionary biologist Richard Dawkins's concept of the "extended phenotype" (Jain et al., 2015).

Digital phenotyping's relation to biology

This leads to the third and final topic: the relationship between the digital phenotyping community and the neuromolecular gaze still dominating psychiatry (Rose, 2018). Several social analysts have noted that, although digital phenotyping is not directly concerned with the genetic or neurobiological levels, biological vocabulary, metaphors, and references still abound. This near-ubiquitous invocation of the biological has been taken as evidence that the field may drive a "biologisation of digital traces" (Baumgartner, 2021: 7) in which "the biological gains in importance" (Baumgartner, 2021: 10) compared with other dimensions, resonating with longstanding concerns about the medicalization or biomedicalization of psychiatry (Conrad, 2005). Likewise, Birk and Samuel (2020: 1875–76) argued that the field's adoption of the "extended phenotype" concept from evolutionary biology implies a "reliance upon a biological and genomic framework" that "runs the risk of reifying mental disorders as (solely) biological." However, they also pointed out how biological language and metaphors "are perhaps less helpful than those working in the field might intend," suggesting the invocation of the biological might be misleading (Birk and Samuel, 2020: 1882). Specifically, they warned that the language of biomarkers and extended phenotypes conveys the impression that digital traces are "products of underlying biology rather than … markers for complex problems of living embedded within a social, cultural and economic environment" (Birk and Samuel, 2020: 1882). An example that, at first sight, would appear to support this critique is the recent review by Montag et al. (2021b) provocatively entitled: "Show me your smartphone … and then I will show you your brain structure and brain function." Yet, illustrating the field's currently weak relation to "bio," the article concludes that, while psychological/psychiatric science has been quick to incorporate digital phenotyping, very few studies have tried to link this to neurobiology.

In the next two sections, I further analyze Montag et al.'s (2021b) observation, as I discuss in detail how the concepts "extended phenotype" and "biomarkers" have been (mis) used or (mis)defined in efforts to link the digital and the biological. Although there have been concerns about how the two concepts are applied in digital phenotyping, for example, whether "the notion of the extended phenotype applies unambiguously to humans" (Stark, 2018: 210) and whether the language of digital biomarkers runs "the risk of reifying mental disorders as biological" (Birk and Samuel, 2020: 1881), my argument and aim differ: I critique mis- and overstatements about digital phenotyping's biological ontology and epistemology in efforts to, first, offer a reality check of digital phenotyping's claims and frameworks and, second, more clearly delineate its psychiatric gaze and demarcate it from the neuromolecular gaze.

The extended phenotype: Misappropriation of a biological concept

Jain et al. (2015) introduced the concept of the "digital phenotype" in a *Nature Biotechnology* commentary that has become a foundational text and standard reference of digital phenotyping. While the text did not explicitly define digital phenotype, the underlying idea is clear: When humans interact with digital technologies, they leave digital traces that can be exploited for the surveillance and early diagnosis of disease, and for understanding everyday manifestations of illness. Cited examples include the use of Google search data to identify suicidal ideation and of tweets to track insomnia.

Conceptually, Jain et al. (2015) argued that the digital phenotype was an extension of evolutionary biologist Dawkins's (1982) concept of the "extended phenotype." This idea has been repeated by other scholars in the field (e.g. Dagum and Montag, 2019)—even though not all digital phenotypers might concur with it (Torous et al., 2016)—and it is also central to social scientific discussions of digital phenotyping's ontology and epistemology (Birk and Samuel, 2020; Coghlan and D'Alfonso, 2021; Loi, 2019; Stark, 2018). The connection to Dawkins's concept is, however, vague. Jain et al. (2015: 462) referred to Dawkins's thesis as being "that phenotypes should not be limited just to biological processes, such as protein biosynthesis or tissue growth, but extended to include all effects that a gene has on its environment inside or outside of the body of the individual organism." They illustrate this with Dawkins's classic claim that dams built by beavers are part of the beavers' extended phenotype. They then go on to argue that human interaction with digital technology can be conceptualized similarly: "As personal technology becomes increasingly embedded in human lives, we think there is an important *extension* of Dawkins's theory—the notion of a 'digital phenotype' [emphasis added]" (Jain et al., 2015: 462). However, this rather grossly misrepresents Dawkins's argument, which is mainly about genes *preserving themselves* by means of their extended phenotype. As later emphasized by Dawkins (2004: 379):

> A beaver dam, and the lake it creates, are true extended phenotypes insofar as they are adaptations for the benefit of replicators (presumably alleles but conceivably something else) that statistically have a causal influence on their construction. What crucially matters … is that *variations* in replicators have a causal link to *variations* in dams such that, over generations, replicators associated with good dams survive in the replicator pool at the expense of rival replicators associated with bad dams. Note what a stringent requirement this is … The beaver's dam is as much an adaptation as the beaver's tail.

We should ask therefore what genetic replicators are maximizing their survival and spread in the gene pool by means of online searches or tweets? How do online searches or tweets increase evolutionary fitness? Are there genes "for" specific digitally recorded behavior that proliferate because they confer evolutionary advantage? Jain et al. (2015) never pose, let alone answer, such questions. In fact, the digital phenotype examples they advance are better conceptualized in terms of what Dawkins (2004: 379) calls "niche changing"—that is, as by-products of our way of life (like *actual* footprints) with no clear evolutionary implications. Therefore, they should not be viewed as extended phenotypes.

Philosopher Michele Loi (2019) seems aware of such conceptual problems but, in an attempt to salvage the idea of the digital extended phenotype, suggested: "bracketing its genetic reductionism" (p. 157). For Loi, the notion of the extended phenotype is useful because it helps digital phenotypers think about how humans produce digital information and about this information's effects (see also Coghlan and D'Alfonso, 2021). Loi (2019: 159) called this a metaphoric use of the term based on "a non-*literal* extension of the original (genetic) concept found in Dawkins [emphasis in original]." However, such a metaphorical use strips away precisely all that Dawkins was advocating, namely, a gene-centric explanation of animal behavior rooted in his adaptationist view of Darwinian evolution (see Gould, 2002: 638–641). Dawkins (2004: 377) is very clear on this point: "Extended phenotypes are worthy of the name only if they are candidate adaptations for the benefit of alleles responsible for variations in them." As Loi (2019) has convincingly argued, however, there is little reason to believe that most of our digital "footprints" (like our actual footprints) are there to enhance certain genes' Darwinian fitness. It is then also inappropriate to view the digital phenotype as an extended phenotype, even metaphorically, unless we want to accept an impoverished definition unrelated to Dawkins's thesis and his broader argument from biology.

Digital biomarkers: Redefining a biological concept

In contrast to the tenuous use of the extended phenotype concept, the use of the term "digital biomarkers" presents a more difficult case to criticize. First, because the use of the parent term "biomarker" has not been very consistent in the literature (Califf, 2018), one might also expect inconsistency in the use of the term "digital biomarker." Second, discussions of what is meant by digital biomarkers are still ongoing, with some authors advocating more stringent use of the term (Au et al., 2021; Babrak et al., 2019; Montag et al., 2021a). Despite these caveats, what I seek to show is that current definitions and uses of "digital biomarker" involve a significant shift in what "bio" in biomarker is taken to denote—specifically, that "bio" now denotes "marker *of* biology," including any digital markers of biology, rather than, as before, "marker derived *from* biology," such as a biomolecule.

What is "bio" in biomarkers?

Biomarker is short for a biological marker, and the concept has been widely used since at least the early 1980s, especially among cancer and environmental health researchers (Lynch et al., 1985). Until recently, a common denominator of definitions was that the "bio" referred to some measured characteristic of biological systems or samples and that "marker" referred to the capacity of that measurement to

signal with high accuracy some *other* biological characteristic, often at a higher level of biological organization.

Historically, one set of influential definitions of biomarkers developed within toxicological research in the 1990s. In the late 1980s, the US National Research Council (NRC) subcommittees for environmental health were tasked by the US government with evaluating the status of biological markers in toxicology. The NRC subcommittees arrived at a self-professed broad definition of biological markers as "indicators of variation in cellular or biochemical components or processes, structure, or function that are measurable in biologic systems or samples" (Henderson et al., 1987).

Subsequently, the WHO, in its environmental health publication *Biomarkers and Risk Assessment* (WHO, 1993), drew explicitly on the NRC definition; later, the WHO defined a biomarker slightly differently as "any substance, structure or process that can be measured in the body or its products and influences or predicts the incidence of outcome or disease" (WHO, 2001). Within environmental health research, the biomarker concept was refined, as researchers sought to apply it in practice. It seemed particularly important for researchers to demarcate "biomarker" from related concepts such as "bioindicator" and "ecological indicator," which were used for measures at the level of whole organisms or ecosystems. For example, one highly cited commentary on the use and definition of these terms in ecotoxicology defined biomarkers as:

> … any biological response to an environmental chemical at the below-individual level, measured inside an organism or in its products (urine, faeces, hairs, feathers, etc.), indicating a departure from the normal status, that cannot be detected from the intact organism. Thus, we want to restrict the term biomarker to biochemical, physiological, histological and morphological (including appearance, pigmentation, surface deformation, etc.) measurements of "health" and exclude behavioural effects. (Van Gestel and Van Brummelen, 1996: 220)

In biomedicine, the idea that biomarkers represent measurements of biological organization at the below-individual level seems almost self-evident given biomedicine's emphasis on the molecular and cellular mechanisms of disease. From the 1990s, associated with many novel clinical and laboratory biotechnologies such as immune, molecular sequencing, and imaging technologies, many biomedical researchers, especially those studying cancer (Nelson et al., 2014), became involved in seeking and evaluating biomarkers. Although a biomarker could be any informative biological marker, in practice, biomarkers were often viewed narrowly as "disease-associated molecular changes in body tissues and fluids" (Poste, 2011: 156). This *molecularized* view of biomarkers is, for example, still evident in the US National Cancer Institute's (NCI) definition of a biomarker as "a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease" (NCI, 2022). Likewise, the European Medicines Agency (EMA) offers a molecularized definition of a biomarker as "a biological molecule found in blood, other body fluids, or tissues that can be used to follow body processes and diseases in humans and animals" (EMA, 2022).

In contrast, a broader (i.e. non-molecularized) definition was developed by the US National Institutes of Health (NIH) Biomarkers Definitions Working Group. From the late 1990s, the Working Group incorporated leaders in the field of clinical trials and biostatistics from the NIH, the US Food and Drug Administration (FDA), academia, and industry to develop consistent and comprehensive definitions of biomarkers and related concepts used in clinical research. The Working Group's (2001) publication "Biomarkers and surrogate endpoints: preferred definitions and conceptual framework" has become a standard reference for biomarker research. Consistent with the idea that biomarkers should reflect measurements of biological systems or samples, the Working Group called biomarkers a type of "biological measurement" that emerged from "the use of a wide array of analytical tools to assess biological parameters" (Biomarkers Definitions Working Group, 2001: 91). The examples of relevant biological levels were molecular (e.g. blood cholesterol), anatomic (e.g. tumor size), and physiologic (e.g. heart function). A potential issue for subsequent conceptual development, however, was that although the text clarified that biomarkers were biological measurements, the formalized definition of a biomarker is ambiguous on this point:

> Biological marker (biomarker): A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. (Biomarkers Definitions Working Group, 2001)

This definition is ambiguous because the biological ontology of the measured characteristic remains undefined. On the other hand, the ontology is arguably implicit in the concept of "biological marker"; moreover, as noted, the biological ontology is explicit in the text as a whole which describes molecular, anatomic, and physiologic measurements as biomarkers. In the context of the dominance of a molecular gaze in medicine, and of a neuromolecular gaze in psychiatry,[1] this ambiguity does little to destabilize the ingrained idea that biomarkers are biological indicators of other (typically higher-level) biological processes (Houle et al., 2010).

Furthermore, in 2016, a joint FDA-NIH Biomarker Working Group formulated an updated definition that seemed to clarify the relevant levels of biological organization encompassed by the biomarker definition and to distinguish biomarkers from behavioral and functional measures.

According to the FDA-NIH Biomarker Working Group (2016), a biomarker is:

> A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or biological responses to an exposure or intervention, including therapeutic interventions. Biomarkers may include molecular, histologic, radiographic, or physiologic characteristics. A biomarker is not a measure of how an individual feels, functions, or survives.

In sum, as late as 2016, the consensus was that biomarkers were *biological markers* with predictive capabilities, with some organizations, such as the NCI and the EMA, going so far as to restrict the definition to molecular markers only.

What is "bio" in digital biomarkers?

However, it is also around this time that the concept of "digital biomarkers" started becoming widely used in academia, industry, and government. Some proposed digital biomarkers in psychiatry may fit a traditional biomarker definition, and some may prove clinically useful. However, as argued below, the currently casual and variable use of "digital biomarker" obscures the fact that neither most digital measurements nor most mental health outcomes are biological in any commonly accepted use of the term.

Starting with academia, one early definition was proposed in January 2017 by the journal Digital Biomarkers (2017) in its inaugural issue:

> Digital biomarkers are defined as objective, quantifiable physiological and behavioral data that are collected and measured by means of digital devices such as portables, wearables, implantables, or digestibles. The data collected are typically used to explain, influence, and/or predict health-related outcomes.

It should be noted that this is simultaneously a narrow and a broad definition. It is narrow because it excludes data that are *not* physiological and behavioral. This definition would, for example, exclude much research on digital biomarkers in oncology, where the concept has been used to describe the results of digital image analysis of tumor morphology that correlate with cancer treatment response (Laury et al., 2021). In general, it would exclude genetic, molecular, cellular, and anatomical data that could be collected for the purpose of digital phenotyping (Bhugra et al., 2017) as well as digital data not collected using personal digital devices, such as electronic health records (Davidson, 2020).

On the other hand, the definition is very broad with respect to both the predictor (i.e. the marker) and the outcome variables to be predicted. Thus, virtually *any* behavioral data that can be collected using a digital device and that correlate with *any* health-related outcome could be a digital biomarker. And in the context of the ever-increasing digitization of healthcare and everyday life, the "behavioral" data seem almost limitless. For example, in psychiatry, the concept has been used to describe how home visits—measured using a visit detection system—may be a biomarker of geriatric depression (Schutz et al., 2021), how the frequency of social media app use among outpatients may be a biomarker of a generalized anxiety disorder (Ryu et al., 2021), and how skipping the use of a breathalyzer, which is connected to a smartphone by an app, may be a biomarker for assessing alcohol use disorder (Zetterström et al., 2019).

Note that some digital phenotypers stretch the biomarker term even further—that is, any kind of digitized data, not only physiological or behavioral data, can become a biomarker (Au et al., 2021). Accordingly, several researchers have used Internet search activity (Birnbaum et al., 2020), social media posts (Adler et al., 2022), geo-location data (Fraccaro et al., 2019), and computer or mobile-device gaming (Johannes Dechant et al., 2021) to derive digital biomarkers of mental health. Using similar logics, because students' GPA scores are associated with mental health, it is not far-fetched to imagine that the proposed digital measures of orderliness (i.e. showering and having meals) and diligence (i.e. entering/exiting the library and fetching water in teaching buildings) (Cao et al., 2019) could be considered promising digital biomarkers.

It should also be noted that—as with the biomarker concept—both the EMA and FDA have been trying to influence the use and definition of the term digital biomarker. This is important because many companies are seeking to develop, use, and commercialize digital biomarker technology (BIS Research, 2020), and many seem to be promoting a broad or even very broad understanding of the digital biomarker concept (Al-Faruque, 2022). For example, a broad definition has been adopted by IQVIA, the world's largest health data analytics and business intelligence company. IQVIA calls digital biomarkers "novel, objective and quantifiable, patient-generated measures of physiology, behaviour, cognitive function and mood that are captured via connected digital devices" (Gores and Baydar, 2021: 1). Notably, compared with, for example, the definition provided by the journal *Digital Biomarkers*, IQVIA adds functional and emotional measures as potential digital biomarkers. However, some companies go *significantly* further. For example, Innovation Sprint has developed a clinical trial digital tool with "digital composite biomarkers" that combine 66 parameters of lifestyle behavior to predict patients' quality of life (Kyriazakos et al., 2021). According to a published study, Innovation Sprint combines (1) various digital measures of sleep and physical activity with (2) data from responses to digital surveys

covering an extremely broad range of non-biological variables: (A) "telephone use, shopping, food preparation, housekeeping, laundry, transportation, medication adherence, and financial management"; (B) "different symptoms" possibly related to medication toxicity; (C) psychological constructs, that is, "fighting spirit," "helplessness/hopelessness," "anxious preoccupation," "fatalism," "denial/avoidance," and a "distress thermometer"; and (D) a "malnutrition score" (Kyriazakos et al., 2021: 8).

However, when faced with such disparate and broad (or even very broad) understandings of digital biomarkers, the regulators' terminological concern appears to relate mainly to the expanding meaning of "marker" and the occasional inclusion of subjective measures, such as surveys (Al-Faruque, 2022; Anonymous, 2020). In 2020, the EMA published its own definition, similar to that of the journal *Digital Biomarkers*, but with an added emphasis on the need to demonstrate "clinical meaning":

> A digital biomarker is an objective, quantifiable measure of physiology and/or behaviour used as an indicator of biological, pathological process or response to an exposure or an intervention that is derived from a digital measure. The clinical meaning is established by a reliable relationship to an existing, validated endpoint. (EMA, 2020: 4)

Likewise, the FDA recently stressed that digital biomarkers, like all biomarkers, should be objective measures that reliably predict a relevant biological or clinical endpoint (Vasudevan et al., 2022). However, unlike the EMA, the FDA's formalized definition remains silent about whether these digital measures should be of any particular *sort* (e.g. physiological and behavioral). For the FDA, a digital biomarker is any:

> characteristic or set of characteristics, collected from digital health technologies, that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. (Vasudevan et al., 2022: 1)

Contrary to the FDA's claim that this definition helps "align the meaning of 'digital biomarker' with established biomarker terminology" (Vasudevan et al., 2022: 1), that is, the NIH-FDA biomarker definition of 2016, the definition arguably supports the ongoing reinterpretation of the meaning of "bio" in biomarker. This is because it is unclear what precisely "bio" denotes in the FDA's definition of digital biomarker—if anything, "bio" seems to relate to the biological or clinical endpoint. Add to this the statements of top FDA staff suggesting that the FDA has no problems also viewing clearly non-biological measures, such as social contacts, as potential biomarkers. For example, in a 2017 interview published in the inaugural issue of *Digital Biomarkers*, Robert Califf, then former (2016–2017) and now current (2022–) FDA commissioner (who between these two terms was Google/Alphabet's head of medical strategy and policy), was quoted as saying (see also Califf, 2018):

> I think social biomarkers like the tone of your voice, the way you ask questions on search, your physical location, and the people with whom you associate—those are going to be great biomarkers. We obviously have work to do there in terms of confidentiality and security, but it's no question, those will be tremendous biomarkers of human health. (Dorsey and Califf, 2017: 94)

Most significantly, in this example, as in many others from digital biomarker publications, the "bio" in biomarkers no longer refers to the ontological properties of the marker but to the ontology of the outcome predicted. It is important to note that this fundamental shift in meaning is not generally associated with a strong argument that digitized behavioral or social measures *are* biological. Instead, it is a shift that appears to occur without justification or even acknowledgment, as if no meaningful shift has occurred.

One can bring home these points using a recent review of digital biomarker definitions by Montag et al. (2021a), who work across academic psychiatry and the digital biomarker industry. Consistent with my argument, their unquestioned departure point is that the "bio" refers to the biological nature of the outcome. They accordingly write: "Many researchers understand that digital biomarkers describe digital footprints providing insights into healthy and pathological human (neuro-)biology" (Montag et al., 2021a: 2). Given this, their concern is now that the outcomes predicted, especially in the mental health field, are rarely (neuro)biological but reflect psychological or behavioral assessments based on expert consensus—a well-known concern of many research psychiatrists (Bhugra et al., 2017). As a solution, they propose distinguishing between *direct* digital biomarkers whose digital footprints are used to predict *bona fide* biological variables, and *indirect* digital biomarkers that predict behavioral variables (e.g. some psychiatric score threshold) and from which "a clinical outcome or underlying biology might be sensed" (Montag et al., 2021a: 4).

More broadly, what this final example also brings home are the fundamental shifts in meaning, and the associated conceptual work needed to accommodate "the biological" within a digital framework, and vice versa. A biomarker no longer means a biological marker; in the best case, it now means a marker of biology. However, in psychiatry, even this latter meaning is contested because of the ambiguous epistemic status of its diagnostic categories and outcomes (Bhugra et al., 2017).

Discussion

In this article, I built on recent empirical and conceptual work examining digital phenotyping to query a proposed epistemic shift in psychiatry. Drawing on Rose and Abi-Rached's (2013) notion of the "neuromolecular gaze," it was suggested that the digital phenotyping thought community is the source of a new psychiatric gaze that I termed the "digital gaze." Rather than privileging neuromolecular explanations, because they represent a deeper truth about human behavior, the digital gaze privileges the "deep" physiological, behavioral, and social "truths" afforded by digital technologies and big data analytics. Equipped with such "deep truths," the digital gaze entails new ways of seeing, judging, and acting upon human normality and abnormality. Whereas the neuromolecular gaze shifted research away from the behavioral and social sciences, the digital gaze seems to offer a shift back. However, this shift is associated with a particular digitized view of the social that embraces continuous and ubiquitous digital surveillance aimed at informing behavioral prediction and effective behavioral modification from afar (Kitchin, 2014).

As often noted in social scientific work on digital phenotyping, it is important to approach digital phenotyping's claims and visions with a critical mindset, as they could reflect hyperbolic expectations common to many future-oriented, high-tech fields. Indeed, it is possible to extend this argument to digital phenotyping's (mis)use and (mis) definition of biological concepts: that they are part of a novel field's exaggerated rhetoric. As such, digital phenotyping might be helped by some counterbalancing reality checks (Choudhury and Slaby, 2016). In delivering such a reality check, this article sought to show that the epistemic link between "the digital" and "the biological" is weak in much digital mental health research to date, notwithstanding the language of extended digital phenotypes and digital biomarkers. Put bluntly, most described digital footprints are *not* extended phenotypes and most proposed psychiatric digital biomarkers are *not* biomarkers; rather, they are digitized physiological, behavioral, and social correlates of mental health experts' constructs. Consequently, one finds little evidence of a biologization of digital traces in which people's digital "brain prints" would somehow be interpreted in light of their biological data. Instead, I propose that digital phenotyping for mental health has so far been engaged primarily in reifying physiological, behavioral, and social traces consistent with what Stark (2018) called psychometric algorithmics.

However, although reality checks are important in the context of overtly simplified or misleading claims, especially when used to justify powerful technologies and expertise (Rose, 2018), it is also clear that such claims can play positive roles in advancing research, especially in a research program's early phase, as shown by the sociology of expectations (Borup et al., 2006). Similarly, historian of science Evelyn Fox Keller (1995) has investigated the role of scientific theories, language, and metaphors in creating productive or stagnating research programs, respectively. Specifically, she analyzed how the discourse of "gene action," despite the paucity of early data supporting the nature of such action, nevertheless allowed genetics to become organized into a productive research undertaking that ultimately led to the deciphering of the structure of DNA (Keller, 1995). Likewise, many have noted that neurochemical theories and imaginaries, such as the monoamine theory of depression, which were "born" already refuted, helped create and sustain productive intellectual and organizational frameworks for psychiatric research in the second half of the 20th century (Healy, 2009; Moncrieff, 2008; Mulinari, 2012). Analogously, the language of extended phenotypes and digital biomarkers may be advancing digital mental health research despite arguably being misleading, for example, by helping secure funding or offering heuristic frameworks in research (Mulinari, 2018).

Indeed, this potentially useful role, at least in the short-term, may help explain why there seems to be a little critical examination of the use and misuse of biological concepts and language in the field. Notably, in the case of the digital biomarker concept, the arguably often pseudo-biological framing is supported by commercial actors with vested interests in digital phenotyping (Cosgrove et al., 2020b). Perhaps more surprising is that drug regulators, in efforts to accommodate "the digital" within regulatory frameworks, are contributing to the unacknowledged and unexplained shift in the meaning of *bio*markers. Most importantly, this article suggests that this remarkable and apparently successful rebranding of the biomarker concept across academia, industry, and government is evidence of a shift in gaze away from lower-level molecular processes towards those higher-level physiological, behavioral, and social processes that can be surveilled using digital devices.

Acknowledgments

The author wishes to thank Francis Lee and Alicja Ostrowska for their comments and careful reading of an earlier version of the text.

Declaration of conflicting interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by a grant from the Wallenberg AI, Autonomous Systems and Software Program—Humanities and Society (WASP-HS) program (no. 2019. 0235, PI Francis Lee).

The funder had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

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Note

1. For example, in psychiatry, Kraemer et al. (2002: 654) stated that "the 'bio-' in the term biomarker refers to any measurable characteristic of living tissue, including those measured by bioassays of blood, urine, cerebrospinal fluid, and skin; by biopsy or autopsy results; by electrical characteristics as measured by electroencephalogram (EEG) or electrocardiogram (ECG), or by structural and functional imaging techniques." Similarly, Singh and Rose's (2009: 202) review refers to psychiatric biomarkers as "biological means of predicting not only the development of a disorder but also its course and outcome"; key examples include physiological markers (e.g. skin connectivity and brain activity), genetic markers, and endophenotypes (i.e. intermediate traits in the chain of causality between genes and diseases).

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