OPINION ARTICLE

How the study of digital footprints can supplement research in behavioral genetics and molecular psychology [version 1; peer review: 2 approved]

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Abstract

Studies that apply digital phenotyping and mobile sensing strategies have increased in recent years enabling a better understanding of psychiatric and psychological conditions, as well as neurodegenerative disorders. Although in this context the study of so-called "digital biomarkers" is proliferating, few studies have actually linked digital footprints to biological variables (and when done, the primary focus lay on brain imaging data). It is well established that many psychological phenotypes such as personality, but also psychiatric and neurodegenerative disorders, have a genetic basis – to a different heritability extent. Therefore, in the present opinion article we argue that it is of tremendous importance to also link the field of neurogenetics to the study of digital footprints, as the latter gives myriad insights into human life and in an objective way. The large field of behavioral genetics including the discipline of molecular psychology could profit greatly from focusing more on the actual study of behavior instead of solely relying on self-report data of study participants. In order to push this promising field forward, the present theoretical work presents three exemplary scenarios, highlighting where such a combination of digital and genetic data could be fruitful.

Keywords

Digital Phenotyping, Mobile Sensing, Molecular Psychology, Personality, Intelligence, Cognitive Ability, Depression, Dementia Neurodegenerative Disorders, Digital Footprints, Neurogenetics, Digital Biomarkers, Psychoinformatics

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Any reports and responses or comments on the article can be found at the end of the article.

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Competing interests: For reasons of transparency Dr. Montag mentions that he has received (to Ulm University and earlier University of Bonn) grants from agencies such as the German Research Foundation (DFG). Dr. Montag has performed grant reviews for several agencies; has edited journal sections and articles; has given academic lectures in clinical or scientific venues or companies; and has generated books or book chapters for publishers of mental health texts. For some of these activities he received royalties, but never from gaming or social media companies. Dr. Montag mentions that he is part of a discussion circle (Digitalität und Verantwortung: https://about.fb.com/de/news/h/gespraechskreis-digitalitaet-und-verantwortung/) debating ethi-cal questions linked to social media, digitalization and society/democracy at Facebook. In this context, he receives no salary for his activities. Finally, he mentions that he currently functions as independent scientist on the scientific advisory board of the Nymphenburg group (Munich, Germany). This activity is financially compensated. Moreover, he is on the scientific advisory board of Applied Cognition (Redwood City, CA, USA), an activity which is also compensated. At the moment he also receives funding a research project on digital phenotyping by Mindstrong Health, Mountain View, CA, USA. JDE notes that he receives royalties for several books published on posttraumatic stress disorder (PTSD); is a paid, full-time faculty member at University of Toledo; occasionally serves as a paid, expert witness on PTSD legal cases; and receives grant research funding from the U.S. National Institutes of Health. PD is the founder of Mindstrong Health, a company developing digital phenotyping products for mental healthcare delivery. He served as its Chief Executive Officer from its founding in 2013 through October 2019 and was granted five U.S. patents on digital phenotyping and digital biomarkers. PD is currently co-founder and CEO of Applied Cognition developing diagnostic and therapeu-tic solutions for Alzheimer's disease. PD owns stock in Mindstrong Health and in Applied Cognition.

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Background

Roughly 65% of the global population has access to the Internet (Internetworldstats.com, 2021). In 2022, it is estimated that there are six billion smartphone users and four billion social media users. With the rise of the Internet of Things (Kopetz, 2011) – a completely connected digital environment – many scientists from different disciplines started to study digital footprints arising from human-machine-interaction to predict psychological and psychiatric variables (Baumeister & Montag, 2019; Insel, 2017; Insel, 2018). To illustrate recent research endeavors, the field among others demonstrated that digital footprints can provide insights into psychological variables such as personality (Montag *et al*., 2016; Montag & Elhai, 2019) or mood disorders such as major depression (Jacobson *et al*., 2019; Saeb *et al*., 2015; Saeb *et al*., 2017) and bipolar disorder (Brietzke *et al*., 2019; Saccaro *et al*., 2021; Zulueta *et al*., 2018). In addition to the interest shown by psychological and psychiatric sciences in studying digital footprints, the medical sciences have also demonstrated increased interest, especially in line with their focus on neurodegenerative disorders, for instance Parkinson's disease (Bhidayasiri & Mari, 2020; Pasluosta *et al*., 2015) or different forms of dementia (Kourtis *et al*., 2019; Montag & Elhai, 2020). Research on the study of digital footprints within the context of brain disorders in general not only aims to establish early warning systems to detect psychiatric and neurodegenerative disorders, but also to use such digital footprints to obtain insights into the course of a disorder, covering the whole spectrum from prevention, intervention and aftercare (see also a recent review paper elaborating on these three areas in the context of Internet Use Disorders; Montag & Rumpf, 2021).

In the brain sciences, it will be of great relevance to not only infer mental states and traits of a person from the available digital footprints, but also to predict a person's underlying neurobiology from patterns of digital footprints left from human-technology-interactions. The current theoretical paper will not review this scarce literature, because this has recently been conducted (Montag *et al*., 2021a). Therefore, at this point in this article we only sum up that work on digital footprints reliably providing insights into the actual neurobiology of a person is nascent and in this context the field mainly has focused on linking data from brain imaging to digital footprints (e.g. Huckins *et al*., 2019; Montag *et al*., 2017). From our view, this is a missed opportunity, because there are different layers of the brain to be studied starting with the molecular-genetic- and epigenetic-basis over endocrinological and immunological variables to the aforementioned brain imaging data including data obtained from magnetic resonance imaging (MRI), electroencephalography (EEG) or positron emission tomography (PET). In the following sections we will focus on the blueprint of the human brain, neurogenetics, and outline why we believe that neurogenetics make an excellent starting point to begin the study of digital biomarkers. Of note, for a debate on the term digital biomarkers see the recent paper by Montag *et al*. (2021b) and for a first feasibility study linking genetic variables to digital footprints see Sariyska *et al*. (2018).

Before we present scenarios where the combination of genetic and digital footprint variables will likely be of great relevance to understand psychological processes and various behavioral variables, we briefly present the current state of affairs regarding the nature-nurture-debate in psychology/psychiatry and neurodegenerative disorders by introducing some prominent examples.

On behavioral genetics, molecular psychology and neurogenetics

It has been proposed that molecular psychology represents an interdisciplinary research endeavor falling into the intersection of personality psychology and biological psychology (Montag, 2017; Montag, 2018). This might be a correct categorization, because on the one hand personality psychologists are mainly interested in understanding individual differences in motivational, emotional and cognitive processes and on the other hand biological-oriented psychologists try to understand how brain processes are linked to these (individual differences in) psychological processes. Moreover, and of relevance, differential psychologists/personality psychologists also have a long tradition of conducting twin studies providing answers to the nature-nurture debate (see below).

In the molecular psychologist's laboratory, the molecular underpinnings (e.g. molecular genetics, epigenetics, endocrinology) of individual differences are the central focus of study-interest and these molecular variables are sometimes combined with brain imaging techniques (Bogdan *et al*., 2017). Logically, the molecular psychologist's work and their investigation techniques can also be exported to study other important phenotypes in psychology ranging from clinical settings (e.g. addiction; Hancock *et al*., 2018), to work and organizational psychology (Montag *et al*., 2015) to social psychological phenomena such as conformity (Deuker *et al*., 2013). For an introduction into concepts and the history of molecular psychology, also see the handbook by Canli (2015). As mentioned in the background section, we will try to present convincing arguments that the molecular psychologist's laboratory could profit from the study of digital footprints. Before we do so, it is worth revisiting some key insights of this still young research endeavor called molecular psychology.

Since the early work of Sir Francis Galton on the heritability of intelligence (Galton, 1891), the study of psychiatric disorders and psychological phenotypes has made a great deal of progress, in particular in recent years. Based on this work it is clear that mood disorders such as major depression, personality traits such as neuroticism (a risk factor for depression, Lahey, 2009) and intelligence are all influenced by many genetic variants, each with small effect size, and environmental factors (Montag & Reuter, 2014; Plomin & von Stumm, 2018). Furthermore, it has also been made clear by abundant research from twin studies that genetics and environment go hand in hand to explain individual differences in susceptibility to psychiatric disorders and psychological traits. Therefore, it is not meaningful to view nature and nurture as distinct entities,

because they influence each other in a highly complex fashion. In the large field of behavioral genetics (comprising both twin study and molecular study approaches), per rule of thumb, genetics and environment each explain 50% of individual differences in psychological/psychiatric traits as has been carved out in a meta-analysis revisiting studies with more than 14 million "partly dependent twin pairs" (Polderman *et al*., 2015, p. 702).

Such findings can be contrasted with insight on the nature of some central nervous system disorders such as phenylketonuria (Pilotto *et al*., 2021) or Huntington's disease (Bates *et al*., 2015), well-known to be autosomal dominantly inherited. Hence, here genetics play the primary role in understanding the medical condition.

Although the study of quantitative traits and monogenetically inherited disorders has made much progress, several problems still haunt the young research field of molecular psychology. Among the problems are difficulties in replicating findings from molecular genetic association studies when dealing with quantitative traits (for instance robustly linking genetic variants to cognitive functions or personality in independent samples, e.g. Ioannidis, 2007) and also that for some neurodegenerative disorders such as Huntington's but also dementia sufficient treatment is lacking (Coneys & Wood, 2020; de la Cruz & Hwang, 2021). In the present work it is argued that with the upcoming study of digital footprints, scientists and practitioners could add a new powerful research resource to their toolbox, which perhaps might even tackle some of the prevailing problems in molecular psychology.

As psychological traits such as personality and cognitive functions, but also different brain disorders, are influenced by genetics to different degrees, the present opinion article provides some ideas below on how the study of digital footprints could supplement the molecular study of the aforementioned brain disorders and related psychological phenotypes.

Scenario 1: *The study of digital footprints likely will help to establish more robust results in molecular genetic association studies*

As mentioned, many psychological and psychiatric traits are at best described by being influenced by both genetics and the environment, and nowadays it is clear that hundreds, if not thousands of genetic markers are of relevance to disentangle the molecular genetics underlying quantitative traits (Montag *et al*., 2020a). In the context of the replication crisis in psychology and the life sciences, molecular genetic association studies in particular have been under fire, as many of the findings from candidate gene studies (and early genome wide association studies) could not be replicated (Border *et al*., 2019). Today, we know that reasons for poor replicability are small sample sizes (large sample sizes are needed to robustly estimate the small effects of each genetic marker), the polygenetic nature also needs to be accounted for to correctly predict genetic risk for psychiatric disorders (Martin *et al*., 2019), and the lack of conceptual overlap when a psychological phenotype is assessed via different questionnaires/methods across studies. The latter point might be tackled in part by relying more on the study of digital footprints. In order to illustrate this with an example, for instance, the major personality risk factor neuroticism for depression can be assessed via different self-report-inventories. It can make a difference though, if neuroticism (N) is assessed via the Eysenck's Personality Inventory or the NEO-inventory, although it is also clear that N-scores assessed via both inventories are robustly associated (perhaps around .80 overlap, hence 64% shared variance; see also Montag *et al*., 2012). From our perspective, the still large non-shared variance of the constructs - even when high correlations between constructs are observed - needs to be considered in the context of the replication crisis when dealing with molecular genetic associations. In short, genetic effects might tap into shared- or non-shared variance of investigated psychological concepts. A classic meta-analysis by Sen *et al*. (2004) underlines this point and revealed that the prominent molecular genetic marker 5-HTTLPR of the serotonin system (Canli & Lesch, 2007) was only related to neuroticism as assessed via the NEO-inventories, but not with other anxiety related personality traits.

When one aims to study the molecular underpinnings of cognitive functions, it becomes even more problematic, because whereas personality is assessed economically often via self-report, ability-factors at best are objectively tested via test batteries. This poses a problem, as it is usually more time-consuming to recruit large numbers of participants for lab experiments than to ask participants to fill in a (short) questionnaire. As the participant-requirements for genome-wide-scan-studies often lie in the area of > 100,000 participants, researchers interested in the molecular underpinnings of intelligence heavily rely on proxies of cognitive functions, e.g. a simple measure such as educational attainment (Okbay *et al*., 2016; Rea-Sandin *et al*., 2021). But how precise is such a measure of educational attainment to obtain fine-grained insights into cognitive abilities of a person (for more insights see Deary *et al*., 2007; Hegelund *et al*., 2020)? In such a scenario, we believe that it would be highly valuable to ask thousands of participants to download an application to allow monitoring of their smartphones to gain insights both into their personalities and cognitive functions, as has been shown in existing research (Dagum, 2018; Montag *et al*., 2019; Sariyska & Montag, 2019; Stachl *et al*., 2017). Cognitive functions could be assessed via reaction times or word usage, when typing messages, and personality could be inferred among others from social activities on the smartphone or social media (see also a meta-analysis on links between personality and Facebook data; Marengo & Montag, 2020). Relying on passively recorded data of the smartphone would also be an advantage, because smartphone-tracked variables might be better comparable than personality assessed via different questionnaires when comparing studies from independent groups (although standardization processes on how long to track a person and so forth are still a matter of debate). Recent work by Montag *et al*. (2022) made the case that through the study of digital footprints as recorded in smartphone-log- or social-media-data *behavioral personality traits* might be established, which perhaps will also result in a modification of

existing taxonomies such as the Big Five, with the latter only relying on a lexical approach (Montag & Elhai, 2019).

Although it is not an easy task to obtain bio-samples and digital footprints from a person, we believe that large centers such as the UK biobank (Canela-Xandri *et al*., 2018) would be able to re-contact participants in their data banks and ask them to also donate their digital footprints to bring the study of molecular underpinnings (going also beyond genetics) of human brain processes and behavior to a new level (for an exemplary tracking app see the work by Montag *et al*. (2019)).

Scenario 2: *The study of digital footprints in persons at higher vs. lower genetic risk for a certain outcome such as Huntington's disease or late onset Alzheimer's disease will help to establish early digital diagnostic markers perhaps performing as well as a genetic test*

In scenario 1 we formulated how the study of digital footprints could be used to enhance the study of quantitative traits by relying not only on self-report information, but directly recorded behavior. Please note that self-report will not be completely obsolete in the near future for many reasons (see Montag *et al*., 2022), but it also would be a wasted opportunity when the study of human behavior in the age of the Internet of Things would still exclusively rely on self-report-questionnaires, which are hampered by problems such as participants answering in a socially desirable way or lacking introspective skills (Paulhus & Vazire, 2007). In the world of the Internet of Things, where everything spoken or not spoken will be recorded, one could ironically ask: Why should we still rely in such a world on self-report questionnaire data, when in principle spoken words and thoughts already exist, although not in a structured, but at least in an unstructured way? For such a scenario, Montag *et al*. (2022) already made the case for contrasting self-report questionnaire data and objectively recorded speech/behavioral data to search for (in-)congruencies, which might reveal interesting insights into (clinical aspects of) human nature.

This said, we believe that not only in the molecular study of psychological phenotypes such as personality or cognition, the introduction of digital footprints could be of merit, but also in the molecular study of neurodegenerative disorders (Kourtis *et al*., 2019; Montag & Elhai, 2020). To illustrate this idea, in the following we contrast Huntington's disease (HD) and late onset Alzheimer's. HD represents a neurodegenerative disorder belonging to the group of movement disorders. HD represents an autosomal dominant inherited disorder, where "alleles of $(CAG)_{40}$ and above are fully penetrant and cause Huntington disease within a normal lifespan, whereas alleles of $(CAG)_{36–39}$ confer an increasing risk of developing Huntington disease" (Bates, 2005, p. 768–769). Furthermore, it has been put forward that a greater number of CAG-repeats go along with an earlier onset of this disorder (Langbehn *et al*., 2010).

Late onset Alzheimer's disease (LOAD) in contrast represents a neurodegenerative disorder being both influenced by genetic risk markers (Karch *et al*., 2014), but also environmental influences (Dosunmu *et al*., 2007). Carrying the so-called epsilon 4 allele (resulting from the combined genotypes of two SNPs on the APOE gene; Montag *et al*., 2014b) is associated with elevated risk for LOAD (Michaelson, 2014), whereas on the side of environmental factors among others an active lifestyle, not smoking and low alcohol intake have been established as protective factors (Lee *et al*., 2010).

Given differences in heritability pathways in HD and LOAD, the application of digital footprints in related research might result in slightly different research agendas. In both scenarios it might be interesting to see if the genetic risk for the neurodegenerative disorders can be inferred from digital footprints such as reaction times changes over a longer time period (perhaps to the extent that distinct behavioral patterns as observed in the digital data might be diagnostic indicators as good as a genetic test). And it clearly can make a difference if the onset of the neurodegenerative disorder can be stopped or at least postponed via means of pharmacological or other interventions or if this is not possible at all. Here, the study of digital footprints could also serve as early detector systems of disease progress, which might be accompanied by appropriate behavioral and/or pharmacological interventions. For an overview regarding interventions in HD and LOAD see the following works (Bucknell Bossen & Kottasz, 2020; Dickey & La Spada, 2018; Yao *et al*., 2011).

Scenario 3: *Searching for gene by digital footprint (as an environmental variable) interaction effects might explain more variance in a psychological / psychiatric phenotype*

In a third scenario we discuss if the combination of information on genotypes and digital footprints outperforms diagnostics relying only on genotypes or digital footprints. This might be true in particular for brain disorders or psychological phenotypes being influenced by genes and the environment. Whereas in the autosomal dominantly inherited HD the genetic information can precisely predict if a person will suffer from HD, diagnostics of other brain disorders such as major depression could benefit from the combination of information regarding both genetic and environmental variables. According to the diathesis-stress-model (Arnau-Soler *et al*., 2019) it is often argued that genetic risk plus adverse environmental factors such as childhood trauma or recent stress could heighten the risk of developing a brain disorder (Lesch, 2004; Sullivan *et al*., 2000). On the other hand, additional gene by environment constellations are discussed, such as that positive environmental influences (e.g. support by one's own social network) might help to reduce the genetic risk and onset of a disorder (Montag & Hahn, 2018; Reiss *et al*., 2013). Interventions for mood disorders could involve mindfulness practices and physical activities, which have been shown to prevent the occurrence of mood disorders (Fink *et al*., 2021; Hofmann *et al*., 2010). In sum, the idea of scenario 3 is that the diagnostic process will benefit from the combination of molecular genetic information of a person plus his/her digital footprints to better predict a clinical outcome. This is likely also true for psychological phenomena such as personality, where both nature and nurture are well-known relevant players (but see also limitations, Werme *et al*., 2021).

Until now, environmental factors often have been assessed via self-report questionnaires. In particular, when retrospectively assessing childhood trauma (Bader *et al*., 2009; Bernstein *et al*., 2003), the study of current digital footprints clearly cannot help to collect information on crucial exposures that affect mental health, as they happened in the past. Nevertheless, we think that the rich sensor information on smartphones collecting information on active vs. passive lifestyle (via physical activity patterns; McConnell *et al*., 2017), social support in terms of being contacted each day (hence a sociality factor; Montag *et al*., 2014a), gaining insights into the direct environment of a person such as weather factors (Aram *et al*., 2012) and noise levels (Miura *et al*., 2019) are all relevant to be studied in light of gene by environment interaction models. In sum, in scenario 3 we aimed to outline the potential to search for gene by digital footprint interaction effects on a myriad of psychological and psychiatric variables which would supplement the often-studied gene by environment investigations until this day, where the latter most commonly have been assessed via self-report.

Summary and limitations

The present theoretical research piece aimed to highlight why the fusion of neurogenetics with the study of digital footprints will likely open up new and exciting avenues to shed light on brain disorders and psychological traits in the context of molecular psychology and behavioral genetics (the latter as the overarching discipline). In this work we presented three scenarios, where we imagine how such fusion might be meaningful. Of course, these scenarios are just exemplary, and we could easily think of additional research settings, where the combination of molecular and digital data is meaningful. In particular the study of epigenetics (methylation patterns/histone modification/mRNA levels) from our perspective will profit from adding a digital layer with information on a person's lifestyle to the epigenetic data to search for meaningful covariations.

Although the combination of the here aforementioned variables has the potential to improve our understanding of the human mind and perhaps also the treatment of devastating human conditions in the area of psychiatry and neurodegenerative disorders, both the study of digital footprints and molecular genetics come with special responsibilities in terms of data protection and privacy (Dagum & Montag, 2019). Hence, strict procedures should be followed to protect the rights of patients/study participants and to make sure that the research we presented, for instance, is not used to decide upon the price of an insurance policy. Without trust in digital phenotyping and mobile sensing procedures, progress will be hindered in this exciting new field (Markowetz *et al*., 2014; Montag *et al*., 2020b). Beyond this, many layers of the human mind await exploration in the context of digital footprints. However, neurogenetics is a logical start from a bottom-up perspective on the human mind, and the fusion of neurogenetics with digital footprints will need to be enhanced by the study of epigenetics, hormones, brain imaging and so forth. Only by taking into account the different layers of the human mind - also in light of the study of digital footprints left from human-machine-interaction – will it be possible to obtain a more precise picture of our brains from which psychological functions arise (Cobb, 2020). The brain sciences including molecular psychology likely will profit from the study of digital footprints. Therefore, we close this paper optimistically with words borrowed from an article investigating experimental approaches to the study of anxiety (Markett *et al*., 2014): We are "in favor of behavior" (p. 1).

Data availability

No data are associated with this article.

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Reviewer Report 20 September 2022

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✔ **Chrsytalina Antoniades**
Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

Montag and colleagues do a great job of emphasising the importance of linking digital footprints to the study of neurogenetics.
In particular, this paper focuses on molecular psychology outlying 3 potential scenarios where such a combination might provide useful information. This is a nicely written and well-thought-through article providing a lot of interesting information using a clever way to engage the reader.

The scenarios are nicely laid out and a good way to approach this area. For instance scenario 2 which focusses on neurodegenerative disorders such as HD and AD is of great interest. In the case of HD, there is a very well-defined premanifest period. In some cases, this can be years, and this can be done since there is a well established blood test that can detect the number of CAG repeats for each individual.

The authors have done a great job putting this article together and I feel that it is very relevant in the current area of digital phenotyping. I highly recommend it for passing peer review.

Is the topic of the opinion article discussed accurately in the context of the current literature?
Yes

Are all factual statements correct and adequately supported by citations?
Yes

Are arguments sufficiently supported by evidence from the published literature?
Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?
Yes

Competing Interests: I was an author of a chapter of a book that Christian Montag was an editor of. However this has not affected my ability to provide an impartial review for this article.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 June 2022

https://doi.org/10.21956/molpsychol.18676.r26798

Yu-Hsuan Lin
Institute of Population Health Sciences, National Health Research Institutes, Miaoli County, Taiwan

The article summarized how digital footprint can be applied as a novel research tool in the field of behavioral genetics and molecular psychology. The authors provided three detailed practical scenarios in which digital footprints can be used to demonstrate the benefits of adopting this tool in a research. The article provides unique insights that could help researchers who are interested in this field to have a clearer picture of how to apply digital footprints as research tool. One issue I notice in this article is that the article didn't mention how to handle data with different time scales, which is a common problem one might encounter when adopting digital footprints as research tool. Despite the issue mentioned above, the article provides unique insights and concisely summarizes the potential of digital footprints. Hence, I would recommend this article.

Is the topic of the opinion article discussed accurately in the context of the current literature?
Yes

Are all factual statements correct and adequately supported by citations?
Yes

Are arguments sufficiently supported by evidence from the published literature?
Yes

Are the conclusions drawn balanced and justified on the basis of the presented arguments?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Digital psychiatry, mobile health, cyberpsychology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.