WHITEPAPER:

The Pulse of a Cough

Your Heart Reacts to Every Cough - Exploring Correlations Between Cough Frequency and Heart Rate

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Executive Summary

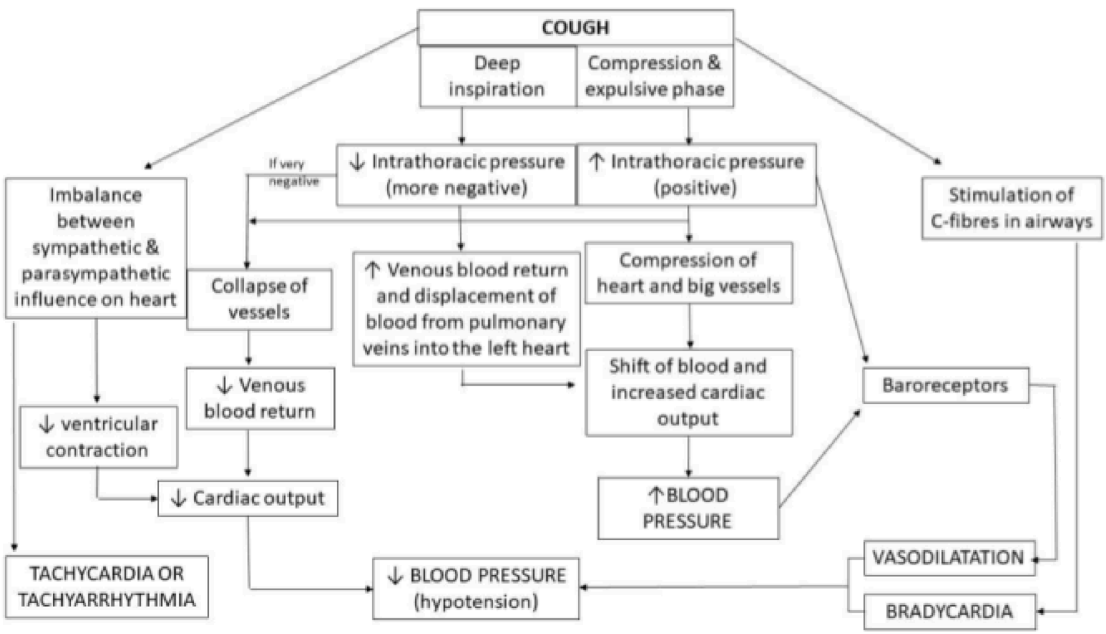
This white paper describes a pilot study that assessed the changes in heart rate before and after cough in 24 healthy volunteers. We demonstrate significant cough to cough variability within individuals and distinct patterns of average changes in heart rate between different individuals. We hypothesize that the chronotropic effect of cough may reflect an individual's autonomic and hemodynamic status. We suggest future avenues for research to better understand the physiology of cough chronotropicity.

The variability in the chronotropic effects of cough revealed in this study suggests that such simultaneous monitoring of heart rate and cough could provide valuable insights into autonomic function, disease progression, and patient well-being. These findings open avenues for integrating continuous, unobtrusive monitoring into both clinical trials and consumer health applications.

The Hyfe CoughMonitor Suite, with its powerful AI-powered cough detection and availability of additional sensors, including HR, is well-positioned to enable these advancements in both medical and wellness contexts. If there is scientifically valid utility in understanding the chronotropic effect of coughing the Hyfe device could be modified to provide this information unobtrusively and continually for wellness or medical uses.

Introduction

It has long been appreciated that coughing impacts cardiac rate. As shown in Figure 1, this is likely due to a complicated interaction between hemodynamic and autonomic pathways. Thus we hypothesize that a more nuanced understanding of the chronotropic effects of cough may provide information on an individual's physiologic state. This pilot study explored the chronotropic effect of cough in 24 health volunteers and suggests that future studies using continuous monitoring of cough and heart rate would be a promising approach to understand and exploit this phenomena for wellness or clinical applications.



Cough as a Cause and Consequence of Heart Dysfunction - Current State of Art Physiol. Res 69, 2020

Figure 1. *Autonomic and hemodynamic interactions with cough*

Heart rate monitoring is a fundamental tool in healthcare, offering valuable insights into a patient's cardiovascular health. Continuous monitoring can detect arrhythmias, assess stress levels, and guide treatment plans for various conditions[1]. The advent of wearable technology has made heart rate monitoring more accessible, allowing real-time data collection outside clinical settings[2]. This accessibility enhances patient engagement and enables early detection of potential health issues.

Cough monitoring is equally important[3], especially in managing respiratory diseases[4]. Objective measurement of cough frequency and intensity aids in diagnosing conditions such as asthma, chronic obstructive pulmonary disease (COPD), and chronic cough. Advanced technologies, including acoustic cough monitors and smartphone applications, have improved the accuracy and ease of cough monitoring[5]. These tools provide clinicians with valuable data to assess disease progression and treatment efficacy.

Assessing cough severity is crucial in clinical practice because it directly impacts a patient's quality of life. Severe coughing can lead to complications like musculoskeletal pain, sleep disturbances, and social embarrassment[6]. Accurate assessment of cough severity helps clinicians tailor treatment strategies, monitor response to therapy, and make informed decisions about patient care.

Various indicators are used to evaluate cough severity, both clinical and technological[7]. Clinically, patient-reported outcomes such as the Leicester Cough Questionnaire and visual analogue scales are commonly used[8]. Technologically, cough frequency monitors, sound analysis, and cough reflex sensitivity tests provide objective data on

[1] Rajkomar (2019)
[2] Dunn (2018)
[3] Smith (2010), Spinou (2014), Birring (2008), Gabaldón-Figueira (2022)
[4] Smith (2006), Lee (2023), Altshuler (2023)
[5] Morice (2006)
[6] French (1998)
[7] Vernon (2009), Raj (2007). Chang (2003)
[8] Birring (2003)

cough severity[9]. Combining subjective and objective measures offers a comprehensive assessment of the patient's condition.

Heart rate monitoring could potentially serve as an indicator of cough severity[10]. Coughing can induce physiological responses, including transient increases in heart rate due to autonomic nervous system activation[11]. Studies have suggested that severe or frequent coughing episodes may correlate with significant heart rate fluctuations. Monitoring these changes could provide additional insights into the impact of coughing on the cardiovascular system, especially in patients with existing heart conditions.

Integrating heart rate monitoring with cough assessment tools may enhance the evaluation of cough severity. By simultaneously tracking heart rate and cough events, clinicians can better understand the physiological burden of coughing on patients. This integrated approach could be particularly beneficial in managing patients with comorbid respiratory and cardiovascular diseases, allowing for more personalized and effective treatment strategies. However, until now there are no experiments related to directly measuring heart rate before and after a cough event.

Understanding cough's physiological burden is critical in both drug development and patient management. In clinical trials, cough-related endpoints are subjective and imprecise, limiting their utility. This study demonstrates a potential biomarker - cough chronotropicity - that could provide an objective, continuous measure for assessing drug efficacy, disease severity, and autonomic function.

[9] Birring (2003), Gabaldón-Figueira (2022)
[10] Wei (1982), Wei (1983), Benditt (2005)
[11] Dockry (2021)

Methodology

The Polar H10 device

The Polar H10 is an ECG-based heart rate sensor that uses electrical sensors to track the heart's electrical activity during contractions. Worn around the chest with a strap for direct skin contact, it provides highly accurate heart rate readings, making it ideal for medical purposes and high-performance sports where precision is essential. The device uses a CR2025 battery, which is non-rechargeable but lasts for around 400 hours of use and is easy to replace. It is particularly suited for continuous heart rate monitoring during intense physical activities.

Figure 2. *Polar H10 device*

Experimental Design

To accomplish this, Hyfe developed custom software (in Python) to timestamp cough events and record heart rate via Bluetooth in real time. In this preliminary work 24 subjects wore the Polar device and were instructed to record the precise time at which they forced coughs as they went about usual daily activities. The resulting records of cough times and heart rate over 20 seconds immediately preceding and following their coughs. A single heartbeat was captured every second.

Ethical Considerations

This low risk observational study of adults was deemed exempt from Institutional Review Board review.

Results

The changes in heart rate for each participant are depicted on the Y axis relative to that at the moment of the cough as a function of time on the X axis in seconds before and after the cough (Figure 3). Results for each cough are shown in the faint lines and the average of all coughs in the dark line.

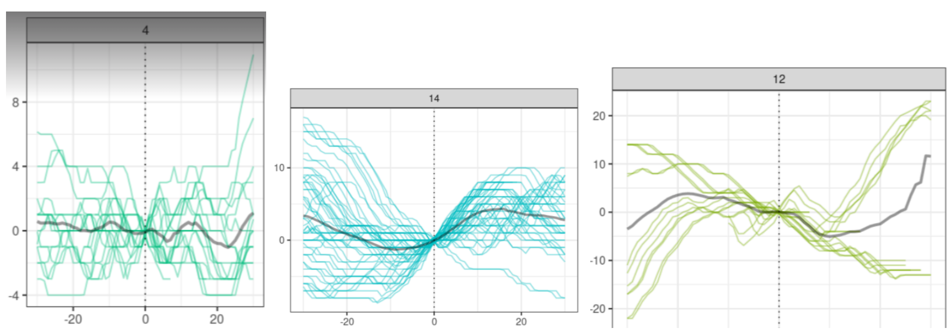


Figure 3. *Data presentation. Changes in heart rate with cough are depicted for each participant on the Y axis relative to that at the moment of the cough as a function of time on the X axis in seconds before and after the cough. Notable is the significant cough to cough variation in chronotropic response for all subjects.*

The first observation that is apparent from Figure 3 is that for all participants there is significant cough to cough variation in the chronotropic response to cough. This amount of cough to cough variability varies between participants. For example, this differs by only 4 beats per minute for Participant #4, as much as 15 BPM for Participant 14 and fall into two distinct patterns in Participant # 12.

While each participant's results are unique, they can be roughly grouped into a few specific patterns as shown in the following Figures.

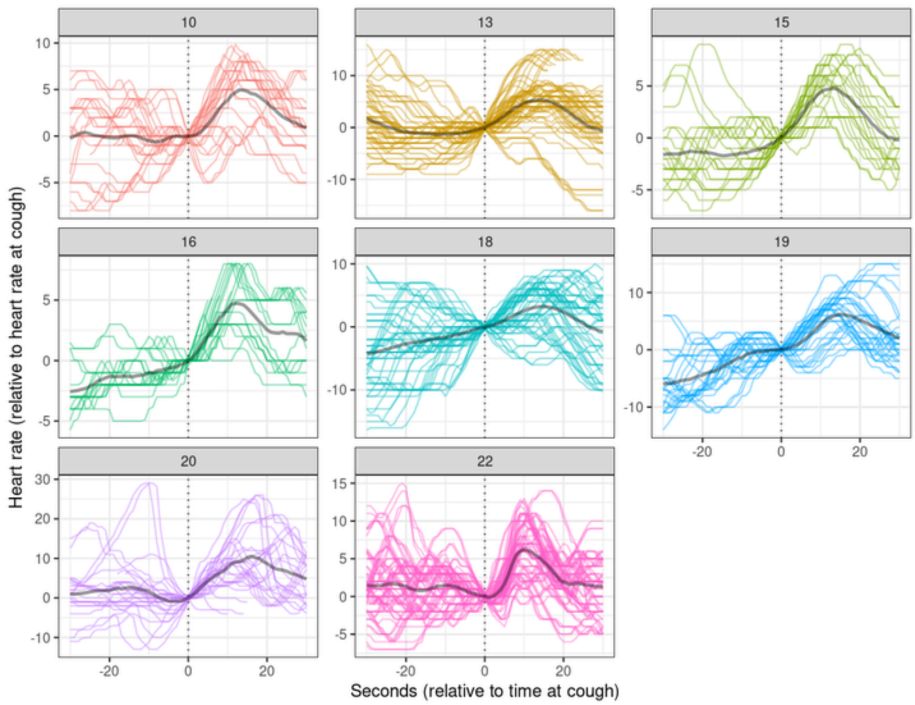


Figure 4. *These subjects show a pattern of average heart rate increases after cough.*

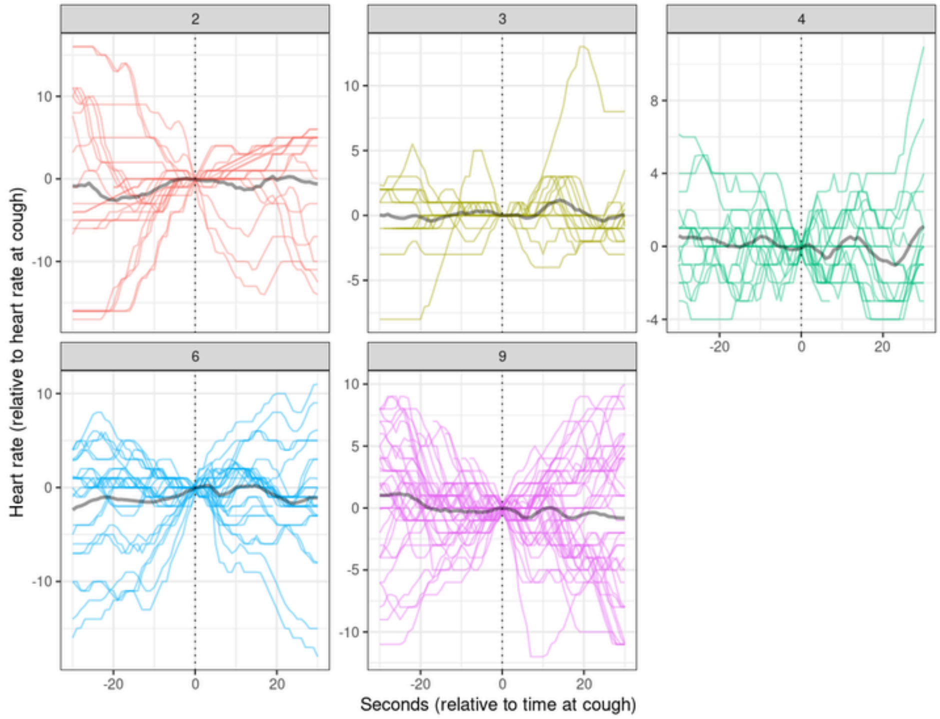


Figure 5. *These subjects show a pattern of average heart rate not changing significantly with cough.*

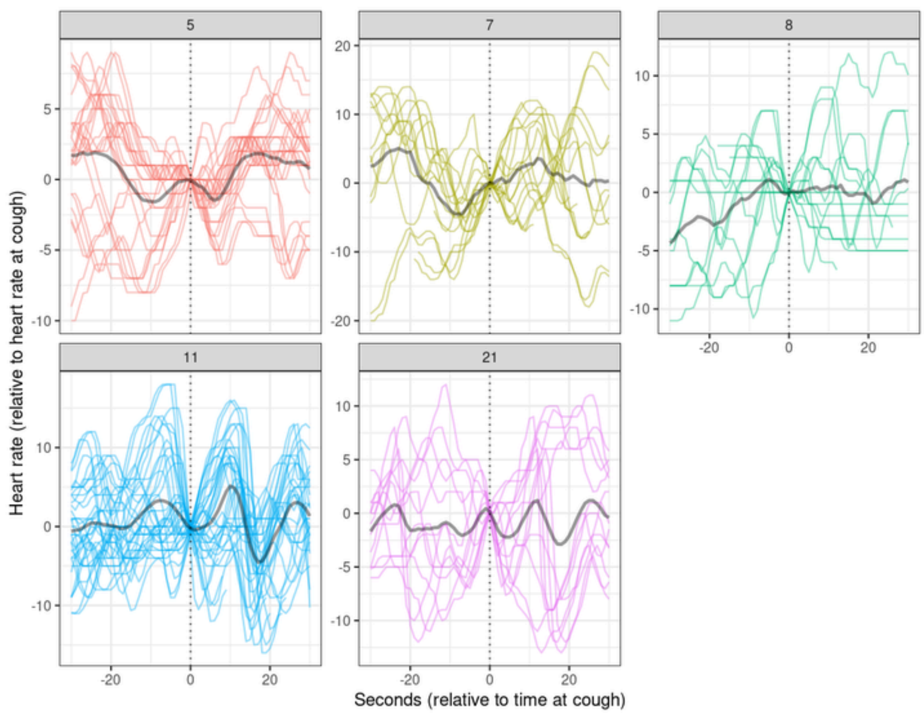


Figure 6. *These subjects show a pattern of average heart rate fluctuating, but not in association with cough.*

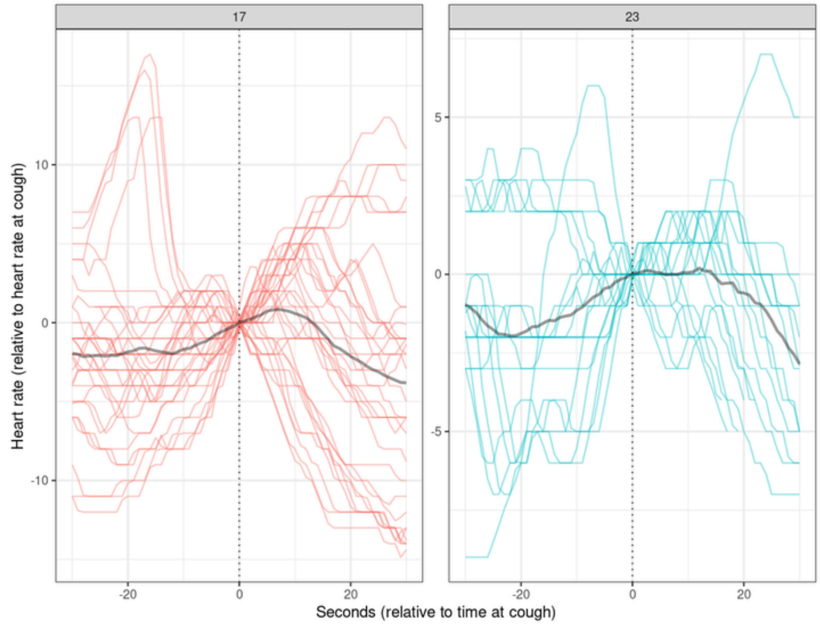


Figure 7.*. These subjects show a pattern of average heart rate increasing before then decreasing after cough.*

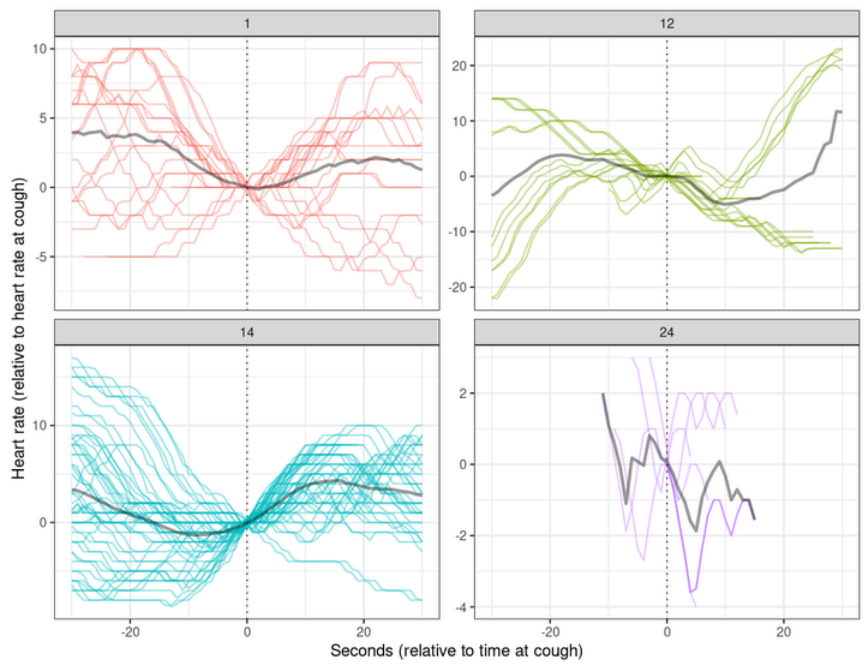


Figure 8*. These subjects show patterns that do not appear to fall into any of the above patterns.*

Discussion

This study, though limited in scope, highlights that cough has measurable cardiac chronotropic effect and suggests that measuring it continuously in real time might provide valuable insights. Research dating back nearly 40 years shows that the chronotropic effect of cough is mediated by hemodynamic and autonomic mechanisms and suggests that its measurement may reflect baseline factors (such as autonomic dysregulation) or transient factors (such as dehydration).

We demonstrated that all participants have significant cough to cough variability in cough induced chronotropic effects. This variability may be explained by a prior study which showed that the hemodynamic effects of cough differ as a function of the pulmonary volume at the time of coughing[12]. The depth of inspiration at the time of coughing was not recorded and may explain some of this variability. Controlling the depth of inspiration prior to coughing in future studies would test this hypothesis.

We also showed that the average change in HR falls into a variety of discrete patterns which may reflect different pathologies or physiologic conditions. In five individuals (20%) participants there was no change in the average HR and in six (25%) the average HR fluctuated but not as a function of cough. An increase in heart rate after a cough, seen in eight (33%) participants was the most commonly observed effect of cough. This cardioacceleratory effect has been previously observed and shown to be diminished with increasing age, presumably a marker for more fundamental physiologic decline. The relationship between age and chronotropicity could also be defined in future studies which control for age.

Categorizing participants into these categories is admittedly imprecise. With a combined dataset of cough and heart rate responses, predictive

[12] LoMauro (2018)

models and unsupervised machine learning algorithms can more objectively categorize responses into specific patterns. When integrated with detailed medical information they may discern correlations with specific conditions.

Assessing the impact of cough on an individual may provide insights into specific autonomic or hemodynamic physiology Currently, autonomic function is assessed by complicated testing, such as tilt table testing. It is possible that assessing cough chronotropicity may provide a simple and continuous measure of this physiology. It is also possible that passive simultaneous monitoring of cough and HR will provide insights into diseases such as cardiac decompensation or cough induced syncope.

A major limitation of this study is that it was a small descriptive study with uncontrolled environmental conditions. As such, the results were likely to be affected by external factors (e.g., movement, stress, or physical activity) which confounded the association between coughing and cardiovascular response. A more controlled study with a larger, diverse cohort would help address these limitations and provide greater insight into the link between cough and heart rate. Alternatively, a massively increased sample size might be informative by averaging these factors over prolonged periods.

Nonetheless, exploring real-time patient-reported outcomes alongside physiological data could offer valuable context, connecting subjective experiences of cough severity with measurable physiological stress.The improved data granularity of these measures may also have applications for clinical trials. This granularity can refine understanding of drug effects on respiratory symptoms, supporting more robust, data-driven insights in trials targeting respiratory diseases and comorbid cardiovascular conditions.

Understanding the relationship between a cougher's subjective experience measured by patient reported questionnaires and objective cough monitoring is an active field of research. The chronotropic effects of cough provide a new framework for this association. Tracking both cough frequency and heart rate may provide a more holistic view of the physiological burden of coughing on patients. We hypothesize that the physical demands of fluctuating or intensified cardiac rate that occurs in chronic coughers hundreds of times a day may contribute to the subjective exhaustion experienced by coughers.

With further research and technological development, integrating cardiovascular monitoring into respiratory assessment protocols could yield novel clinical insights and the quality of care for patients with respiratory and cardiovascular conditions.

Applying AI / machine learning to combined cough and heart rate data could enable automated detection of pathologic patterns, allowing for early intervention in at-risk patients. These insights could be integrated into clinical trial endpoints or digital therapeutics (DTx) and would be particularly well suited for remote and decentralized trials.

The combined tracking of respiratory and cardiovascular health may also have applicability for consumer health applications, where users seek comprehensive, real-time health data. Devices and technologies that integrate both cough and heart rate monitoring can offer unique insights into the effects of respiratory symptoms on fitness and daily activities. For example, athletes and fitness-focused users might leverage this combined approach to monitor the impact of respiratory events on cardiovascular recovery, providing a proactive tool for optimizing health and performance. This integrated approach could be deployed in wearable technology, offering real-time, holistic assessments of patient health. For companies in health quantification, this approach could create a competitive advantage by offering comprehensive health insights that combine respiratory and cardiovascular data.

***Table 1**. Potential Applications of Real Time Assessment of Cough Chronotropicity*:

Assess hemodynamic status	Such as CHF decompensation, hydration status, etc
Assess autonomic status	Augment orthostatic BP measurement and tilt table
Insight into cough severity	Physiologic toll of frequent coughing?
Evaluate specific conditions	Cough syncope

This study highlights the potential of new applications of integrated cough and heart rate monitoring in clinical trials, digital health, and chronic disease management. Future research should focus on refining predictive models, conducting larger controlled studies, and exploring regulatory pathways for medical and wellness device integration. As Hyfe continues to innovate, collaboration with pharma companies, wearable tech developers, and clinical researchers could unlock new opportunities for personalized healthcare.

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