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SCHOOL OF MEDICINE

Thesis

NEUROPSYCHIATRIC CORRELATES OF POWER STATE IN SMARTPHONE USE

by

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A.B, B.E., Dartmouth College, 2012

Submitted in partial fulfillment of the

requirements for the degree of

Master of Science

2019

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ACKNOWLEDGEMENTS

I would first like to thank my thesis advisor and mentor, Dr. John Torous of Beth Israel Deaconess Medical Center at Harvard Medical School, for his support and guidance throughout this research year. He was always available to answer my questions and steer me in the right direction. It has been a pleasure working on the many exciting projects within the Division of Digital Psychiatry this year and I am very grateful for the opportunity.

I would also like to thank my graduate school advisor and thesis reader, Dr. Isabel Dominguez at the Boston University School of Medicine, for supporting me and many of my peers throughout our degree.

I would also like to thank my third thesis reader, Dr. Paulo Lizano of Beth Israel Deaconess Medical Center at Harvard Medical School, for his valuable comments on this thesis. I am very grateful to have had his insight throughout this research year.

Finally, I would like to thank everyone in the Keshavan Lab for being so supportive and always willing to take time out of their day to discuss research or answer a question. I would like to thank Olivia Lutz for not only doing a phenomenal job in managing a large neuroimaging research lab but also for having the patience to teach essential tools in statistics that I needed for my thesis.

NEUROPSYCHIATRIC CORRELATES OF POWER STATE IN SMARTPHONE USE

PHILIP HENSON

ABSTRACT

Schizophrenia is a complex and devastating illness with heterogeneous symptoms, late diagnosis, and excess early mortality. It is also associated with comorbidities including substance abuse, depression, anxiety, and sleep problems, that have adverse effects on the individual over the entire course of the disease. While effects of these comorbidities have been identified in the literature, few studies have involved longitudinal assessments and reproducible data collection in large populations. Recent smartphone research tools have been developed that provide better access to patients and can enable a real-world snapshot of a person's mental state. In addition, these tools use the phone's sensors to construct a digital phenotype of an individual, with the potential to detect changes in symptoms and cognition on a moment-by-moment basis. Previous studies report associations between anxiety and smartphone use, but most involve cross-sectional data and cohorts of healthy controls completing paper and pencil scales. A recent smartphone study collected day-to-day symptomatology, cognition, and phone usage data and discovered that the association between anxiety and smartphone use is more complex than originally thought.

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LIST OF ABBREVIATIONS

app .... application

BACS .... Brief Assessment of Cognition in Schizophrenia

fMRI..Functional Magnetic Resonance Imaging

GAD-7.. Generalized Anxiety Disorder 7-Item Scale

GPS ....Global Positioning System

HC .... Healthy Controls

HIPAA ....Health Insurance Portability and Accountability Act of 1966

IRB .... Institutional Review Board

LAMP .... Learn, Assess, Manage, Prevent

PANSS .... Positive and Negative Symptom Scale

PHQ-9 .... Patient Health Questionnaire

SFS...Social Functioning Scale

SZ...Participants with Schizophrenia

INTRODUCTION

Schizophrenia is a Global Disease with a Substantial Burden on Patients

Schizophrenia is a complex mental disorder with many characteristic symptoms including hallucinations, delusions, cognitive impairment, disorganized speech and behavior, social withdrawal, and low energy (Kahn et al. 2015). It has a lifetime prevalence of approximately 4.0 in 1,000 persons and it is estimated that one in two people living with schizophrenia does not receive appropriate care (Anon n.d.; Saha et al. 2005). These effects are magnified because the decline in social and cognitive functioning associated with schizophrenia can occur in early adolescent years, but the disorder is not often diagnosed until later adolescence or early adulthood (Kahn et al. 2015; Kahn and Keefe 2013). Various comorbidities such as substance abuse disorders, anxiety, and depression may also be present throughout the entire course of the illness, often resulting in poorer outcomes (Buckley et al. 2009). In addition, even after successful treatment, the risk of relapse is ever-present and identifying those risks have proven difficult to identify (Emsley et al. 2013). Furthermore, life expectancy for people with schizophrenia when compared with the general population is on average 20 years lower (Laursen, Nordentoft, and Mortensen 2014). The combination of heterogeneous symptoms, late diagnosis, risk of relapse, and excess early mortality contribute to the severity of schizophrenia and the importance of active care and treatment.

Smartphones Provide a Promising New Platform for Mental Health Applications

Smartphones are increasingly prevalent in today's society, with recent estimates of smartphone ownership around 77% for the general U.S. population and around 69% for young adults experiencing first-episode psychosis (Anon n.d.; Lal, Nguyen, and Theriault 2016). Retention and adherence rates, along with access, have provided promising measures for feasibility of mental health smartphone studies. For example, a review by Firth and Torous (Firth and Torous 2015) found that among several smartphone application (app) trials for schizophrenia, 92% of participants continued the trial until the end and interacted with relevant apps between 86.5 and 94% of the days comprising the study.

One of the main benefits of smartphones is their ability to capture both active and passive data streams. Active data is collected by direct interaction with participants, for example, in filling out surveys, completing cognitive tests, or by drawing images with a finger. Passive data, on the other hand, is collected entirely in the background without any input from the participant and includes global positioning system (GPS), accelerometer, heart rate, step count, and phone screen time. Both active and passive data can be collected at any moment, without a participant necessarily needing to travel to a hospital or clinic. A recent study demonstrated the potential of combining active and passive data streams in the identification of early signs of relapse in people with schizophrenia. In a 3-month pilot study of 17 participants with schizophrenia, Barnett et al. found that among subjects who experienced a psychotic relapse, passive data captured by smartphones identified 71% more abnormalities around the relapse date than

elsewhere (**Figure 1**) (Barnett et al. 2018). The abnormalities, or anomalies, discussed in the study refer to patterns of behavior that deviate from an individual's normal behavior. For example, if someone who makes around five phone calls each day were to quickly shift to a pattern of no phone use, that deviation may be considered anomalous and would be factored into the analysis. Although a small-scale pilot, this study suggests the potential use of mobile monitoring.

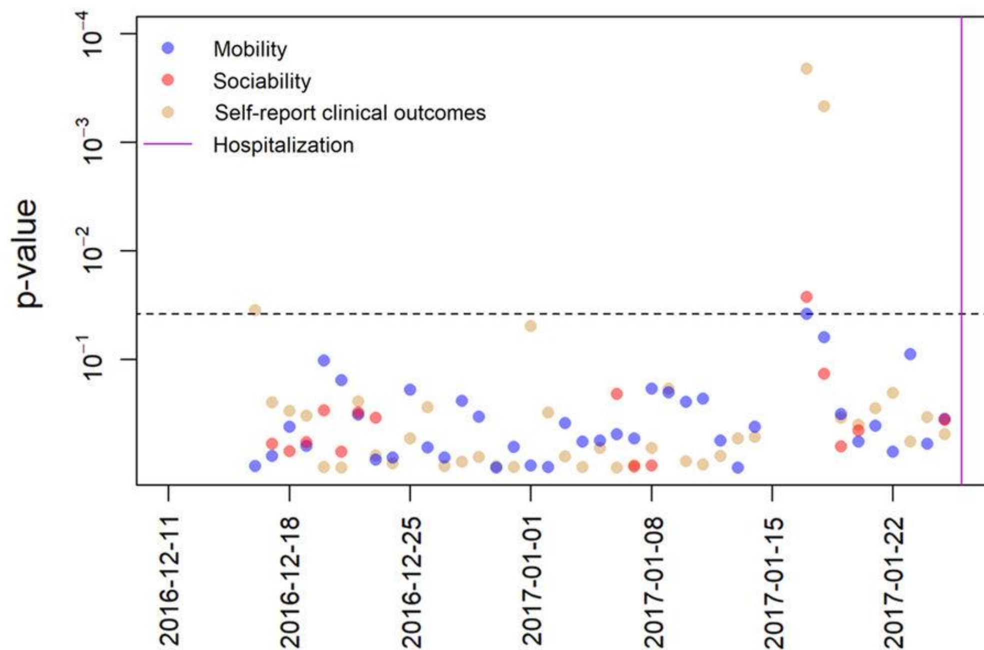

Figure 1. Daily Anomaly Detection Leading Up to Hospitalization for Psychosis Relapse (Barnett et al. 2018)
There were significant anomalies detected (based on a personalized threshold for significance) in each of the categories (mobility, sociability, and self-report of clinical outcomes) within nine days of hospitalization.

Quantifying Comorbidities in People with Schizophrenia

Even in patients who do not experience a relapse, there is a dynamic nature to symptoms over the course of schizophrenia that can change from week to week or day to

day. These symptoms are not always psychotic in nature and are often associated with comorbidities, the most common of which are substance abuse disorders, anxiety, and depression (Buckley et al. 2009). These comorbidities can be present throughout the entire course of the illness and are generally associated with more severe psychopathology and poorer outcomes.

Recently, there is rising concern that screen time is related to adverse mental health outcomes. In youth, there is a significant relationship between screen time and worsening psychological wellbeing, based on results from the National Survey of Children's Health (Twenge and Campbell 2018). While there is no consensus on what exactly constitutes problematic smartphone use, the study found that the threshold for lower psychological well-being was as low as 1 hour per day of screen time. As smartphone ownership increases, this "problematic" screen time becomes closer and closer to phone time. In fact, smartphone use in particular has been associated with adverse mental health outcomes like depression, anxiety, and trouble sleeping (Temmingh and Stein 2015). However, it is still unclear how more phone time or a particular pattern of use may relate to mental health outcomes in patients. In particular, among social media users, there is no statistically significant relationship between social media platform use and symptoms of depression, indicating that responses to phone use are personal and differ based on the individual (Rideout and Fox 2018).

Smartphone studies, with their active and passive data collection, have begun to investigate these comorbidities in schizophrenia. Recently, Huckins et al examined several different data streams to identify relationships among: depression scores on paper

and pencil scales, depression scores on a mobile phone app, functional magnetic resonance imaging (fMRI) of brain connectivity, and mobile phone usage as measured by screen unlock time (Huckins et al. 2018). This study found positive correlations between smartphone screen time and connectivity between the subgenual cingulate cortex and regions of the ventromedial-orbitofrontal cortex, while also demonstrating overlap with self-reported depressive symptoms from both scales. While a proof-of-concept in healthy subjects, this study demonstrates the capabilities of smartphone research in linking every-day behavior and frequent check-ins with symptomatology that could be expanded to patient populations.

While smartphone studies have begun to use modified scales to measure depression (Huckins et al. 2018; Torous et al. 2015), there is surprisingly a lack of research on smartphone measurements of anxiety. A recent meta-analysis found that the mean prevalence of any anxiety disorder in schizophrenia is 38%, but significant heterogeneity among studies with many potential moderating variables make anxiety difficult to quantify (Achim et al. 2011). Others have found positive associations between symptoms of anxiety and severity of both positive and negative symptoms on the Positive and Negative Symptom Scale (PANSS) (Braga, Reynolds, and Siris 2013; Mazeh et al. 2009). Despite this research into the impact and prevalence of anxiety disorders in schizophrenia, the diagnosis and treatment of anxiety symptoms and disorders is still overlooked in the management of schizophrenia (Temmingh and Stein 2015).

Relationship Between Smartphone Use and Anxiety

Smartphone use, often referred to by "power state" in smartphone studies, has previously been associated with mental health symptoms like depression, anxiety, stress, and problems sleeping (Thomee 2018). Specifically with respect to anxiety, relationships have been reported between general smartphone use and anxiety (Lepp, Barkley, and Karpinski 2014), text messaging and anxiety (Billieux, Van Der Linden, and Rochat 2008), bedtime smartphone use and anxiety (Saling and Haire 2016), and excessive or problematic smartphone use and anxiety (Lee et al. 2016; Richardson, Hussain, and Griffiths 2018). However, many of these studies have only been conducted in healthy populations of young people, such as college students, and involve single measurements of self-reported anxiety and phone use. The lack of clinical data, detection of real time dynamic anxiety symptoms, and reproducibility of these cross-sectional studies have left room for new methods of data collection. Smartphone studies with active data collection (e.g. smartphone-delivered surveys) and passive data collection (e.g. screen time representing phone use) have the potential to overcome these limitations, by providing robust data streams for any desired study population. The goal for this thesis is to demonstrate how to combine a single smartphone data stream, screen time, with an important comorbidity of schizophrenia, anxiety, for the first time in a highly reproducible analysis that can in the future be applied to any combination of data streams and symptomatology.

METHODS

The LAMP Platform (Active Data)

The LAMP platform (Learn, Assess, Manage, Prevent) is a smartphone research tool supported by a grant from the Natalia Mental Health Foundation (IRB approval number 2017P-000359, October 12, 2017). The platform consists of an online portal for researchers and a smartphone app for participants. The online portal allows for the creation of research studies and scheduling of cognitive tasks and customized survey questions. The app notifies the participant of the scheduled assessments and records results of survey responses and cognitive tasks as well as time taken for each question response or button press. Results are uploaded from the phone to a HIPAA-compliant server where they can be processed and analyzed. A full description of the platform has been outlined in a manuscript, submitted under the title "The development of a smartphone app designed to improve clinical care based on patient, clinician, and researcher needs," and is currently in academic peer review (Torous et al. n.d.).

The Beiwe Platform (Passive Data)

In addition to collecting active data (e.g. survey responses and cognitive task scores) the study also includes passive data collection through an app called Beiwe. The Beiwe research platform was developed by the Onnela Lab at the Harvard TH Chan School of Public Health with the goal of being a full-fledged platform for the collection of research-quality sensor data (Torous et al. 2016). In our study, the Beiwe app collects

multiple streams of raw smartphone data in the background, including accelerometer, GPS, call and text logs, and power state (i.e. phone usage).

Participants

A total of 79 participants – 35 healthy controls (HC) and 44 with schizophrenia (SZ) – from the greater Boston area who own smartphones enrolled in this IRB-approved research study after signing written informed consent. Of the 79 original participants, 67 provided adequate active and passive smartphone data for analysis (**Table 1**). In particular, the data streams of interest were anxiety scores (GAD-7 composite scores) taken within the LAMP app and phone usage as measured from the power state passive data streams from Beiwe. The phone sensors record when the screen is turned on and off, so daily power state was calculated as the sum of the differences in time between "on" state and "off" state in a given day.

Table 1: Participant Demographics
67 study participants from the greater Boston area who own smartphones generated both passive and active data for analysis

	HC	SZ	p
	24	43	
Age (mean (sd))	23.18 (1.53)	38.29 (14.46)	<0.001
Sex = male (%)	15 (68.2)	22 (56.4)	0.528
Race (%)			<0.001
American Indian or Alaskan Native	0 (0.0)	4 (9.8)	
Asian	20 (83.3)	1 (2.4)	
Black or African-American	1 (4.2)	10 (24.4)	
Multiracial or Other	0 (0.0)	2 (4.9)	
White Caucasian	3 (12.5)	24 (58.5)	
Education (%)			0.001
4-year College Graduate or Higher	21 (87.5)	16 (37.2)	

High School Graduate/GED	1 (4.2)	13 (30.2)
Some College	2 (8.3)	11 (25.6)
Some High School	0 (0.0)	3 (7.0)

Procedure and Data Collection

At the first study visit, participants are explained the types of data collected and sign informed consent. They complete a series of paper and pencil tests including the Patient Health Questionnaire (PHQ-9) for depression, Generalized Anxiety Disorder 7-item scale (GAD-7), the Social Functioning Scale (SFS), the Positive and Negative Symptom Scale (PANSS) (Giesbrecht et al. 2016), and the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al. 2004). Participants then install both LAMP and Beiwe on their smartphones for active and passive data collection, respectively, which they use as much or as little as they'd like for three months. After three months, participants return for a second and final visit where they repeat the assessments and are given an overview of their collected data.

During the three-month period between visits one and two, participants are prompted on their smartphones to take 10 surveys per week (two each of mood, anxiety, psychosis symptoms, sleep, and sociability). Throughout the study, Beiwe is constantly running, collecting power state information every time a phone screen was turned on or off. Figure 2 shows an example of the frequency of data collection for three tracks: accelerometer, GPS, and screen on/off. Presence of color indicates that the sensor is on and data is being collected, and white space indicates those sensors are idle or off and not collecting data.

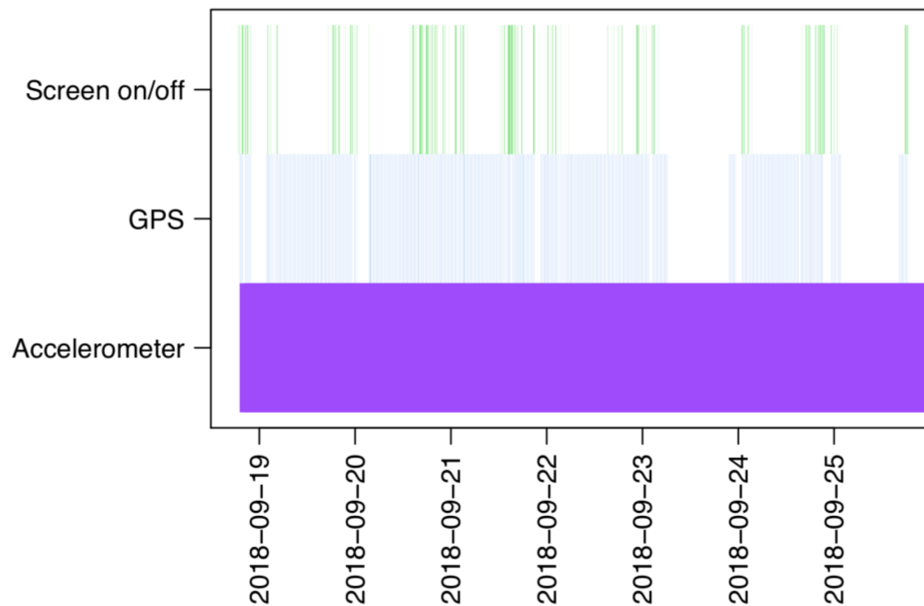

Figure 2: Sample One-Week Collection of Passive Data Streams (Torous et al. 2018) This figure demonstrates the frequency of data collection for three passive data streams for one week for a single participant. In this example, accelerometer data is collected constantly, whereas GPS and screen on/off time (phone use) are collected less frequently.

Statistical Analysis

Analysis was conducted using the R programming language within the application RStudio. Anxiety scores (GAD-7 composite scores) were tabulated daily within the app and averaged when multiple surveys were taken in a single day. Phone use was assessed from the power state information collected by Beiwe and calculated as the difference in time between phone unlock and phone lock. In our investigation of problematic smartphone use, we used a threshold of greater than 60 minutes per day based on findings from studies that investigated the relationship between phone and/or screen time and adverse mental health outcomes (Twenge and Campbell 2018; Zheng et al. 2014).

In addition, we used the statistical approach *k*-means clustering on the data. *K*-means clustering is a straightforward, unsupervised approach and has been used previously in psychiatry research as a way to categorize participants based on large and complex data streams (Clementz et al. 2016; Fuente-Tomas et al. 2019). We used a standard method of *k*-means clustering to categorize SZ into various GAD-7 anxiety groups – Low (0-4), Mild (5-9), Moderate (10-14), and Severe (15-21) – based on age and problematic smartphone use.

A supplementary analysis was conducted using the paper and pencil results of the social functioning scale collected during visit 1 and is displayed in **Figure A** in the **Appendix**.

RESULTS

Anxiety and Phone Use

Linear models were performed on both HC and SZ daily anxiety score as scored in LAMP and daily phone use (**Figure 3**). Each point is a day's worth of data for a single participant and includes at least one anxiety survey as well as passively recorded phone usage data. For SZ, $r^2 = 0.0018$, $p = 0.55$, slope = -0.088 and for HC, $r^2 = 0.020$, $p = 0.52$, slope = -0.033.

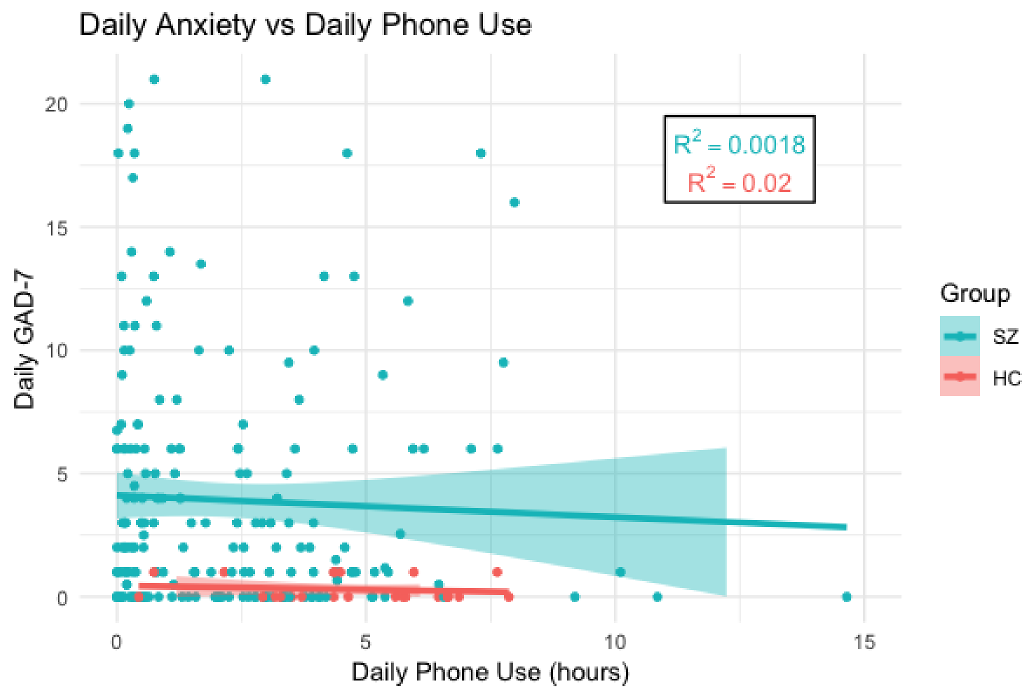

Figure 3: Daily Anxiety Score vs Daily Phone Use
For both SZ ($p = 0.55$, slope = -0.088) and HC ($p = 0.52$, slope = -0.033), low correlations are seen between daily phone time (hours) and daily GAD-7 scores.

Anxiety and Problematic Phone Use

A similar analysis was performed on participants with problematic smartphone use (> 60 minutes) and is displayed in **Figure 4**. For SZ, $r^2 = 0.0025$, $p = 0.61$, slope = 0.10 and for HC, $r^2 = 0.083$, $p = 0.69$, slope = -0.026.

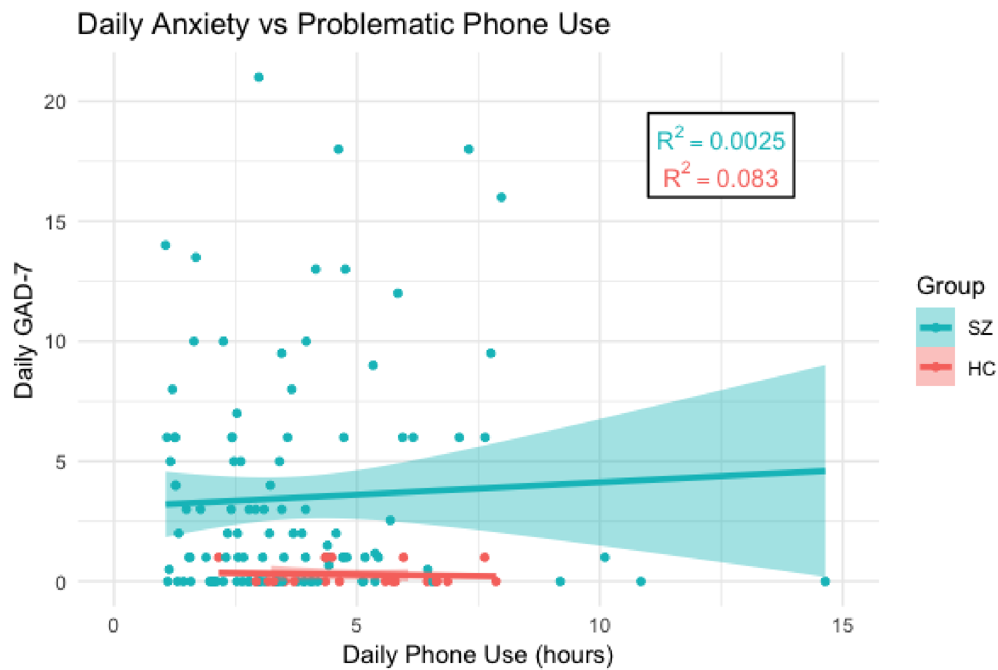

Figure 4: Daily Anxiety Score vs Daily Phone Use (> 60 minutes)
Aside from a change in slope in SZ, daily anxiety and problematic phone use correlations remain low for SZ ($p = 0.61$, slope = 0.10) and HC ($p = 0.69$, slope = -0.026).

Anxiety and Phone Use in SZ: Stratified by Age

A third linear model analysis was performed on different age groups among SZ and results are shown in **Figure 5**. R^2 values for SZ ranged from 0.00032 (p = 0.53) to 0.35 (p = 0.84) and slopes from -0.91 to 2.1

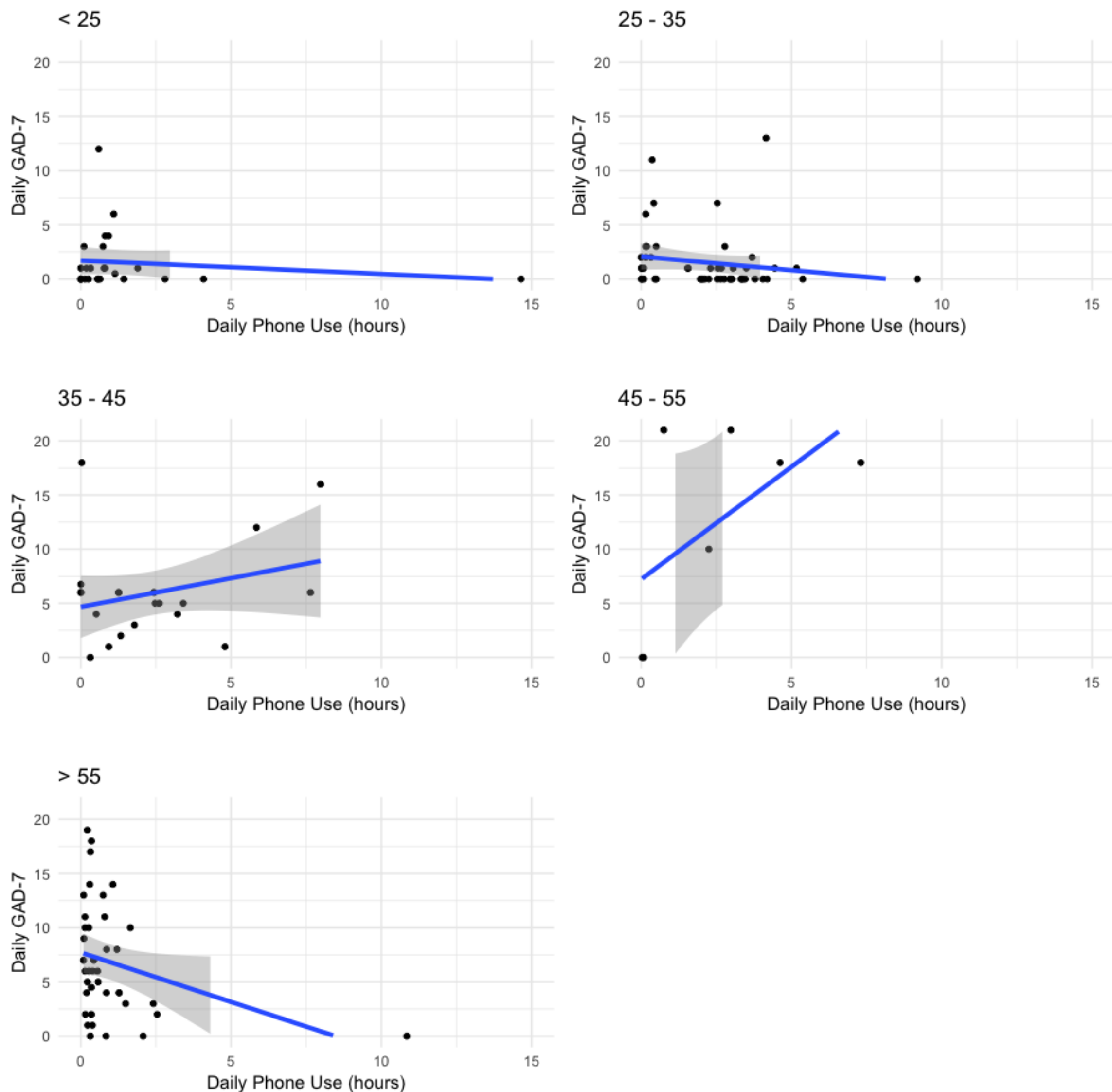

Figure 5: Age Bracket Snapshots of Daily Anxiety vs Daily Phone Use
Stratifying SZ by age shows the heterogeneity of results when investigating the relationship between daily anxiety and daily phone use.

K-Means Clustering on Age and Problematic Phone Use to Predict Anxiety

The clustering process began with cluster dendrogram (**Figure B, Appendix**) from which we determined that three clusters would be sufficient for the analysis. The final table (**Table 2**) shows in which clusters participants were sorted. The clusters demonstrate separation of the groups, with cluster 3 containing mostly participants with low anxiety, cluster 1 containing participants with mild anxiety, and cluster 2 containing participants with moderate to severe anxiety. The results are also represented graphically in **Figure 6**.

Table 2: *K*-Means Clustering Results
The algorithm-defined clusters in the first column represent "buckets" that SZ appear to fall into based on their anxiety severity (GAD-7 composite scores). Columns two through four represent low, mild, moderate, and severe anxiety.

Cluster	<= 4	4 - 9	9 - 14	14 - 21
1	4	**8**	1	1
2	5	1	**3**	**3**
3	**13**	2	1	0

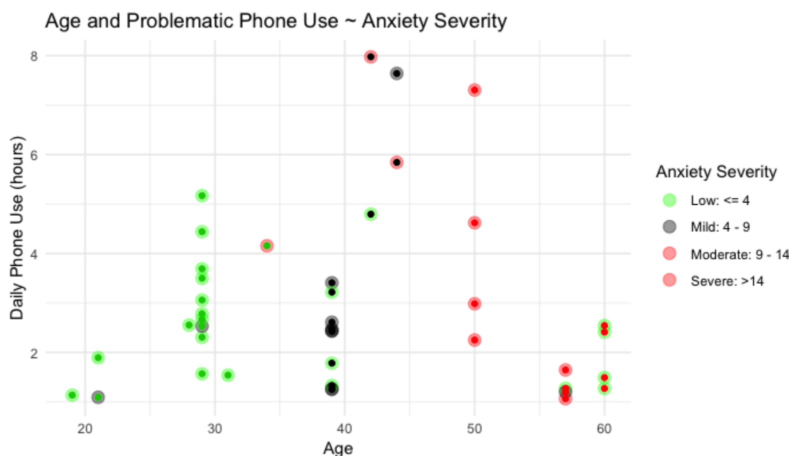

Figure 6: Effect of Age on Comparing Problematic Phone Use with Anxiety Severity
The results from **Table 2** are represented in this plot. Points with the same inner color as outer ring color are classified correctly, whereas points with a different outer color were classified incorrectly.

DISCUSSION

While previous studies correlate anxiety to smartphone use largely based on single, self-reported surveys in heathy controls, new smartphone-enabled survey and power state data collected among participants with schizophrenia demonstrate that the relationship is more complex. Based on the results of the linear model (SZ $p = 0.55$, $r^2 = 0.0018$ and HC $p = 0.52$, $r^2 = 0.020$), no significant conclusions can be drawn about the relationship between daily phone use and anxiety in patients with schizophrenia. When adjusting the sample to include SZ with problematic phone use, the slope of the regression in SZ went from negative (-0.088) to positive (0.10), but the linear model fit still yields an insignificant correlation (SZ $p = 0.61$, $r^2 = 0.0025$ and HC $p = 0.69$, $r^2 = 0.083$).

These results suggest that the relationship between phone use and anxiety in schizophrenia is complex and likely mediated by other factors. Heterogeneity based on age was seen in **Figure 5**, where linear model r^2 values for SZ ranged from 0.00032 ($p = 0.53$) to 0.35 ($p = 0.84$) and slopes from -0.91 to 2.1. In addition, phone screen time may not properly reflect actual phone activity. For example, someone using social media to facilitate social connections may have a different experience than someone playing games on their phone instead of exercising. To partially address this, as a supplementary analysis, we investigated the relationship between social functioning (assessed at visit 1) and phone use (**Figure A, Appendix**). HC ($n = 5$) and SZ ($n = 29$) showed different relationships between social functioning and daily phone use, with slopes of -3.7 and 1.7 respectively. This analysis further demonstrates that phone use in it of itself may not be a

consistent comparator across groups and may be affected by other factors like age and social functioning, which could be controlled for in future studies.

The *k*-means clustering algorithm placed 59% of SZ with low anxiety into cluster 3, 73% of SZ with mild anxiety into cluster 1, and 67% of people with moderate to severe anxiety into cluster 2. Overall, 64.2% of SZ with problematic phone use were clustered correctly. While the linear model correlation was unable to discern a relationship between problematic phone use and anxiety, this clustering method is closer to establishing a relationship by taking age into account, ultimately shedding more light into the contributing factors in the relationship. Another benefit of this analysis is that it is easy to implement and reproduce on additional data sets. A future direction of this research could be to test the clustering algorithm on additional data sets that have daily anxiety scores and daily phone use metrics. Additionally, a similar clustering method could be used to validate smartphone anxiety surveys against clinical paper and pencil surveys. In general, the data collection methods used in this study along with the statistical analysis show feasibility in moving the field forward from cross-sectional studies in small samples with healthy participants into real-time data collection and longitudinal studies in larger populations of both healthy controls and patients.

Limitations

Data Collection

Both active and passive data streams were affected by issues with data collection. Due to the nature of the study, surveys were prompted for participants but not required to

be completed, leading to missing data points. In addition, for some participants, server outages would cause passive data streams to cut off for periods of time, further reducing the quantity of data for analysis. These are important issues to take note of in early studies such as this in order to target for improvement.

Determining Problematic Phone Use

Despite multiple findings for the greater than sixty minutes screen time threshold holding significance in some studies, there is no consensus on whether any amount of screen time constitutes problematic phone use, and the approach taken in this analysis may not fully capture what it means for smartphone use to be problematic. There currently exist robust scales for measuring problematic smartphone use that take other factors into account like dependence, antisocial use, and dangerous driving.(Kuss et al. 2018) A future study might benefit from combining the passive measures of power state with active survey questions on how people use their phones to obtain a more accurate measure for problematic phone use. This direction of research might help set new definitions for problematic smartphone use that are easily usable, sharable, and reproducible.

Conclusion

The relationship between anxiety and phone use is complex and cannot be explained by solely looking at screen time and self-reported surveys. In people with schizophrenia, there may be other contributing factors like age and social functioning. Smartphone

studies have the capacity to collect both active and passive data and are crucial in understanding the dynamic nature of mental illness by capturing day-to-day symptomatology, cognition, and behavior, with the ultimate goal of improving care delivery.

APPENDIX

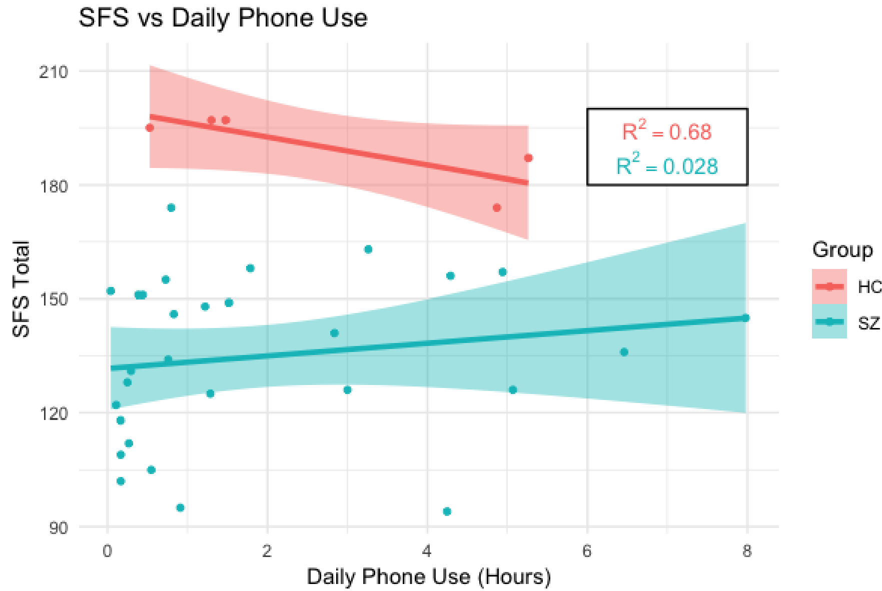

Figure A: Social Functioning Scale and Total Phone Time
Comparing visit one scores for social functioning with daily phone use shows differences between HC (p = 0.086) and SZ (p = 0.39) groups.

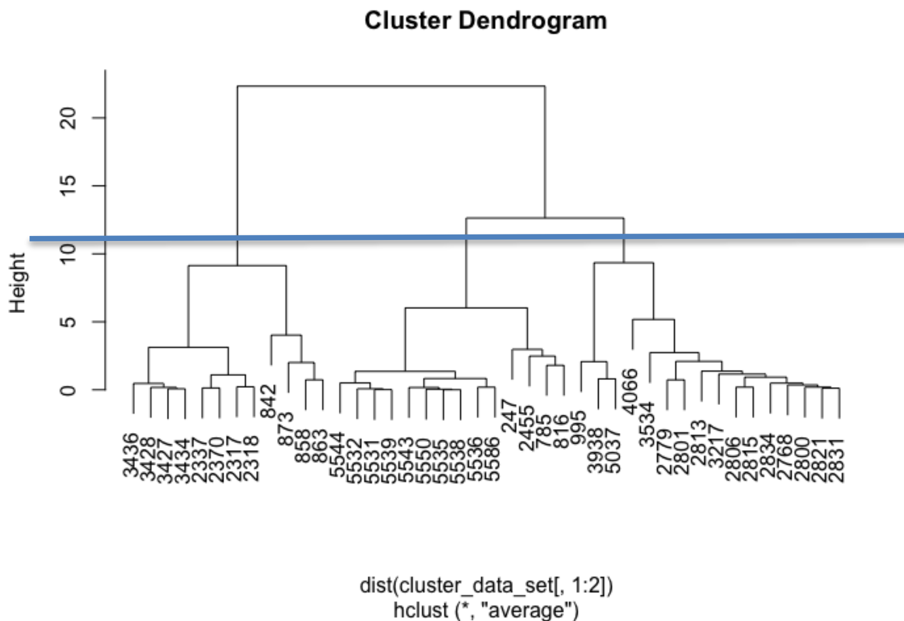

Figure B: Cluster Dendrogram for Identifying Number of Clusters
A cluster dendrogram is one of the first steps for *k*-means clustering and is used to visually determine how many clusters to use (Kodali 2017). The horizontal blue line overlaps three vertical lines, suggesting the use of 3 clusters.

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