**Grant Brief: Examining the Interaction between Demographic and Lifestyle Factors and Impact on Cognitive Performance**

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**Assignment Acknowledgement**

This assignment has a Turnitin originally score of 8%. I attest that I have used the following generative artificial intelligence tools to aid in this assignment: Grammarly to correct grammatical mistakes and Chat-GPT to check a readability score and understand the order of elements according to CIHR.

Lifestyle and Cognition: A Large-Scale Intervention Approach

**Recent Progress**

Over the last 25 years, a suite of computerized tests has been developed within my laboratory to assess aspects of memory, attention, planning and reasoning (1–8). These tests have been validated in patients with anatomically-specific brain lesions (1, 2), in neurodegenerative populations (3, 9), in pharmacological intervention studies (10, 11), and their neural correlates have been well studied using functional neuroimaging in healthy adults (4, 6), and in neuropathological populations (12, 13). Thematically, this proposal builds on a new and exciting opportunity that has emerged as a result of us adapting this battery to run online as the [Cambridge Brain Sciences](https://cac-word-edit.officeapps.live.com/we/cambridgebrainsciences.com) cognitive testing platform ([CBS](http://cambridgebrainsciences.com/)). Now, the tests can be completed over the internet and without formal supervision, opening the possibility of large-scale studies of cognition in the general population. Indeed, they have already been taken more than 8 million times, generating what must be one of the largest databases of its kind in the world.

In this proposal, we will exploit the [CBS](http://cambridgebrainsciences.com/) platform, along with several of the large databases that have already been generated using it, to explore the interrelationship between demographic and lifestyle factors, and cognitive performance on a massive scale. For example, we have already acquired a complete normative database of 75,000 participants who have all provided extensive demographic information relating to background, nationality, education, employment, exercise habits, sleep patterns, religiosity and political views, as well as information about alcohol, cigarette and caffeine consumption. In addition, over the last five years, 1.5 million additional users have completed more than 8 million tests on the [CBS](http://cambridgebrainsciences.com/) platform, yielding another rich dataset that is waiting to be mined for information pertaining to the relationship between performance on tests of cognition and factors such as age, gender, and geographical location, as well as how repeated testing impacts cognition. Most recently, cognitive data from 16,600 people was collected, along with a comprehensive questionnaire that included questions about demographic and lifestyle factors, as well as their sleeping habits as part of our [*World’s Largest Sleep Study*](https://www.cambridgebrainsciences.com/studies/sleep-study) *(*[*WLSS*](https://www.cambridgebrainsciences.com/studies/sleep-study)*)*. At the time of writing, this database remains entirely unexplored, and is the largest study of sleep and cognition in the world to date.

**Objectives**

The short-term objective of this proposal isto use our existing datasets to answer questions about human cognition that would simply not be possible in a traditional laboratory setting. We will go beyond asking whether certain factors (like sleep) impact cognition, and begin testing hypotheses about how various life-style factors and demographic variables *interact* to impact cognition. The vastness of the data will allow us to identify which factors are most crucial for optimal cognitive performance within specific sub-populations, across the lifespan. In particular, by applying techniques from machine learning to identify novel relationships between lifestyle factors and demographic variables, we will generate novel insights about the underlying mechanisms of cognition. In the longer term, the results of these studies will provide a framework within which we (and other scientists) can design and conduct intervention studies, both online and in the laboratory, to further investigate newly discovered relationships between lifestyle factors, demographic variables and their effect on cognitive performance. This unique marriage of bottom-up data-driven discovery that generates testable hypotheses leading to intervention studies, will provide an entirely new paradigm for future scientists to explore human cognition.

**Literature Review**

One of the best predictors of life quality, including academic and work success, levels of happiness and even life expectancy is overall cognitive functioning; the better an individual performs on tests that measure different aspects of cognition (e.g., reasoning, attention, memory, verbal abilities, planning etc.), the better their quality of life (14–17). While most research has focused on changes to cognition following brain injury or disease, cognitive abilities are also significantly influenced by life-style factors such as exercise (18), stress (19), sleep (20) and recreational substance use (21), and certainly vary across the life span from childhood to old age (22). However, most studies that have investigated the link between life-style factors and cognition have been laboratory-based, and have examined only a single life-style factor (e.g., exercise) within a specific population (e.g., the elderly). To really understand the relationship between life-style factors and cognition, large-scale studies are required, which cannot be conducted in a laboratory setting.

My laboratory has a strong track record of using our online cognitive assessment platform to address fundamental questions about the relationship between the brain and cognitive function on a massive scale (7, 8, 23). For example, in 2010, the [CBS](http://cambridgebrainsciences.com/) platform was used to assess the efficacy of commercial brain trainers; the results from 11,000 participants revealed no significant improvement in cognition after 6 weeks of training (8). In 2012, the [CBS](http://cambridgebrainsciences.com/) platform was used to question the validity of the IQ construct; data from 44,000 members of the public collected in a matter of weeks showed that cognitive performance could not be adequately described by a single factor, but is comprised of at least three factors (reasoning ability, short term memory – STM, and verbal performance), that are dependent on dissociable brain networks (7). These two studies, which were published in *Nature* and *Neuron*, respectively, *are absolutely central to the current proposal and are, therefore, included as supporting research materials.* Most recently, we collected data from 16,600 participants (results in prep.) to investigate how sleep and other lifestyle factors affect cognition. These results demonstrate that web-based studies of cognition are not only *possible*, but provide a novel opportunity for assessing the multitude of factors that contribute to healthy cognition on a scale that would be simply impossible using traditional laboratory-based methods.

**Methods**

This program of research will comprise 3 main themes:

***THEME 1 – Sleep and Cognition***

There is substantial evidence supporting the conclusion that insufficient sleep results in impaired cognitive function. Clearly, complete sleep deprivation (SD) has catastrophic consequences for a person’s ability to pay attention and complete everyday tasks, but even partial SD has been shown to negatively impact some aspects of cognition (24–26). While there is consensus that the latter impairs “low level” cognitive functions, like vigilance and alertness, there is considerably less agreement about whether “higher order” abilities, such as STM and reasoning, are also affected (27).

**Study 1.1:** Using the large and globally diverse [WLSS](https://www.cambridgebrainsciences.com/studies/sleep-study) dataset, we will examine how self-reported sleep duration and quality relate to cognitive performance, and whether this relationship depends on age. Participants in the [WLSS](https://www.cambridgebrainsciences.com/studies/sleep-study) completed the Pittsburgh Sleep Quality Index (PSQI) (28) in addition to our online 12-test [CBS](http://cambridgebrainsciences.com/) battery. With multiple regression, we will construct models to predict cognitive test scores from PSQI sleep measures and potential confounds like age, level of education, gender, etc. and their interactions. From previous studies (29), we expect there to be an inverted U-shaped association between sleep and cognition: too little or too much sleep will be associated with impaired performance. When possible, we will validate these findings in independent CBS datasets that also contain sleep-related questionnaire data. What remains to be seen is: what cognitive domains are affected, what sleep parameters result in optimal performance, and how these depend on other factors – like age.

**Study 1.2:** Next, we will launch a large-scale online study like the [WLSS](https://www.cambridgebrainsciences.com/studies/sleep-study), but with an added active manipulation to produce day-to-day variations in sleeping patterns. Participants will complete the [CBS](http://cambridgebrainsciences.com/) test battery on two consecutive days, and use an online diary system to track what time they went to bed, woke up, and how much sleep they had the night prior to each day of testing. Participants will also be encouraged to modify their sleep on the second night, so that we examine whether performance fluctuates from one day to the next based on the previous nights’ sleep. That is, how much less sleep is required to produce a deficit, and does this amount depend on age? Again, we will use multiple regression to predict test scores from sleep diary data, and changes in test scores from changes in sleep patterns. Based on our previously published studies (7, 8), we expect to easily recruit between 5000 and 10,000 participants for this, and for all other new online studies in this application, using the existing [CBS](http://cambridgebrainsciences.com/) infrastructure.

**Study 1.3:** Next, we will take the above testing procedures into the controlled environment of our new six-bedroom sleep laboratory at the Brain and Mind Institute at Western University. Guided by the previous results, we will control how long participants sleep overnight in the laboratory to induce partial or complete SD, and measure changes in cognitive performance. Participants’ sleep and cognition will be monitored at home – using “Actiwatches” to record activity levels and sleep duration, and CBS online testing to track cognition – for three days prior to in-lab SD to ensure normal sleep. Following the in-lab procedure, participants will return to their normal routine, during which we will track their recovery sleep and cognitive functioning. We expect that participants who undergo complete SD will have a more widespread pattern of cognitive impairment than those who experience only partial SD, and that their recovery period will be longer. In addition, we will be able to determine: if different cognitive domains are affected to the same extent by SD, whether complete or partial SD affects these systems differently, how long these functions take to recover and whether these effects are different in younger and older participants.

**Study 1.4:** In the previous experiment, it might be the case that cognitive performance appears to return to normal levels following a single night of recovery sleep. However, behavioural recovery might be supported by compensatory mechanisms in the brain; it has been shown that restorative sleep immediately following SD does not completely return task-induced brain activity to normal levels (30, 31). To investigate how changes in brain function support behavioural performance, we will conduct a functional magnetic resonance imaging (fMRI) study of volunteers performing the [CBS](http://cambridgebrainsciences.com/) tests: 1) before in-lab SD; 2) after a night of complete or partial SD; and 3) after one night of recovery sleep. Within-subject comparisons of task-evoked activity will allow us to examine how brain activity within established brain networks underlying STM, reasoning, and verbal abilities are modulated by SD (7). Furthermore, we will be able to compare partial and complete SD to link behavioural recovery of cognitive performance to changes in brain function after different amounts of SD.

***THEME 2 – Cognitive and Physical Training***

Physical and cognitive training have emerged as promising methods for preserving, and even enhancing, cognition. Long believed to improve only bodily health, physical exercise, has now been shown to also improve cognitive health (32). However, the mechanisms by which physical exercise gives rise to improved cognition, remain unclear – do certain forms of physical exercise (e.g. aerobic) improve some domains of cognition (e.g. memory), more than others? Similar uncertainties also surround the benefits of cognitive or ‘brain training’; repeatedly completing computerized tasks leads to improvements in performance on those tasks, but the extent to which this transfers to other aspects of cognition remains highly contentious. An existing literature comprising studies with small sample sizes, vastly different training programs, and poor definitions of transfer further compound these difficulties (33).

**Study 2.1:** The massive CBS databases provide an immediate opportunity for examining how physical and cognitive training habits within the general population relate to cognition across different domains. For example, is there an optimal amount of physical exercise that is associated with improvements to specific cognitive systems, and if so, do these cognitive systems improve in certain populations (e.g., older adults) more than others? Where cognitive training is concerned, the databases include several key questions that will yield insights about the practices and perspectives of brain trainers in the real world, such as, "Do you believe brain training works?"; "How long have you been brain training?”; “Which brain training programs do you use?". With many participants reporting training for up to five years, we will be able to explore, for the first time, the long-term effects of training on different cognitive systems on a time-scale that would be impossible in a typical laboratory setting. We will also use multiple regression and optimization statistics to determine whether factors such as different training programs, prior expectations and various demographic variables are associated with improved cognition in certain individuals.

**Study 2.2:** To further investigate the potential benefits (if any) of cognitive training, we will conduct a large-scale intervention study online using custom-designed training programs focused on specific cognitive sub-systems (i.e., short-term memory, reasoning or verbal abilities). While we have previously demonstrated (8) that cognitive training imparts no general benefits to cognition, that study utilised a general training program (based on a commercial brain trainer), involving many different cognitive sub-systems. We will design and compare targeted training programs centred around single tasks selected from the [CBS](http://cambridgebrainsciences.com/) battery that are optimized to emphasize specific cognitive domains; in each case, one task will serve as the training task, while the remaining eleven untrained tasks will serve as outcome measures. Because the same twelve tasks will be used in this revolving manner, this approach we will allow us to quantify the degree of transfer based on previously established metrics (7) and to directly compare how training different cognitive sub-systems effects specific and general outcomes, across the lifespan.

**Study 2.3:** Converging evidence suggests that both aerobic and resistance exercise leads to improved cognition (34, 35). However, these findings are typically based on specific subpopulations (e.g., the elderly (36)) using a single measure of cognition (e.g., memory (37)). To move beyond a piecemeal understanding of the relationship between physical exercise and cognition, we will conduct a series of laboratory-based studies whereby we manipulate the type and amount of exercise, in both older and younger adults, and monitor the acute and chronic effects using the [CBS](http://cambridgebrainsciences.com/) platform. In this way, we will examine whether aerobic and strength-based exercise differentially improve cognition and, if so, what aspects of cognition? We will use multivariate multiple regression to generate models that best explain which measures of cardiovascular fitness (e.g., heart-rate variability) and physical strength (e.g., push-ups), contribute most to improvements across different cognitive domains. Moreover, we will examine whether pairing physical exercise with cognitive training optimizes the benefits to cognition. For example, if aerobic exercise improves memory performance, we predict that combining it with a memory centred cognitive training program will produce additive effects beyond what would be expected from each form of training alone.

**Study 2.4:** Differences in the degree of improvements in cognitive functioning after physical or cognitive training across individuals are likely best understood at the neural level. Brain networks (both functional and structural) that underlie different cognitive domains, the degree to which these networks are activated, and the extent to which other networks are simultaneously recruited, may all relate to the success (or failure) of physical (38, 39) and/or cognitive training programs (40–42). To explore how changes in cognition are mediated by changes in brain function and structure, we will use fMRI combined with structural measures such as diffusion tensor imaging (DTI) to examine the brain at specific intervals during an extended period of 1) physical training only 2) cognitive training only, and 3) a combination of physical and cognitive training. We predict that gains in cognitive performance will be associated with more overlap between the functional and structural brain networks that are recruited during training and those mediating outcome; without such an association, there is no mechanisms for transfer to take place.

***THEME 3 – Other Lifestyle Factors and Cognition***

The previous two research themes will address specific mainstream hypotheses about cognition and lifestyle, but there are likely other less obvious relationships that our large [CBS](http://cambridgebrainsciences.com/) datasets are ideally suited to reveal. For example, we recently (7) incidentally observed that some cognitive abilities can be dissociated according to their relationship with specific demographic or lifestyle variables – such as age, gender, level of education, cigarette smoking, region of birth, level of anxiety, and even video game usage. The literature is replete with studies that link such factors, in isolation, to measures of cognition, e.g. (43–45), but the sheer scale of our datasets will allow us to investigate how these characteristics co-vary across the population, and how these patterns relate to specific aspects of cognition and brain function.

**Study 3.1:** The [WLSS](https://www.cambridgebrainsciences.com/studies/sleep-study) dataset includes approximately fifty questions relating to lifestyle and demographics, such as: languages spoken, socio-economic status, level of education, employment, recreational drug use, basic medical history, mental health, diet, hobbies, etc. While one could ask whether there is a pairwise relationship between each individual questionnaire item and each of the twelve [CBS](http://cambridgebrainsciences.com/) test scores, we will seek to identify an underlying structure that relates these two datasets; that is, are there sets of lifestyle and demographic variables that are associated with some combinations of test scores? Multivariate methods, like canonical correlation, will be used to find linear combinations of the variables (i.e., factors) within these two datasets that best explain the variability both within and between sets. We know that at least three cognitive factors explain performance across the 12 [CBS](http://cambridgebrainsciences.com/) tests, and that these factors are not all associated with the same subject variables (e.g., level of education was positively related to STM and verbal ability, whereas video game experience correlated positively with only STM) (7). Therefore, we expect our multivariate analyses to reveal the same three cognitive factors, and, given the prior observations, that there will likely exist a ‘cognitive optimization factor’ (comprised of education, frequency of video game usage, etc.) that is positively related to STM, but not reasoning and verbal, performance. We will further test whether these effects are replicable in an independent data set of 44,000 individuals who were tested on the same [CBS](http://cambridgebrainsciences.com/) battery and a similar questionnaire in 2012.

**Study 3.2:** The [WLSS](https://www.cambridgebrainsciences.com/studies/sleep-study) questionnaire was by necessity very broad yet quick to complete, and hence does not have in-depth coverage for many of the included topics, such as recreational substance use (e.g., coffee, alcohol, etc.). However, it is likely that any relationship between cognitive performance and factors such as these depends on specific details that were not captured by our survey. For example, if long-term cognitive effects exist, they likely depend on the age of onset, duration of use, frequency, and the amount of the substance used (45). To more precisely map these kinds of relationships, we will perform targeted follow-up studies online, examining the variables that were most strongly associated with cognitive performance in Study 3.1 above. A common paradigm will serve each experiment: participants will complete the [CBS](http://cambridgebrainsciences.com/) battery and a questionnaire that will be tailored to that topic. In-depth surveys of existing literature will guide questionnaire creation, so that critical details and confounds will be captured. If possible, an active manipulation will be included to detect an acute modulatory effect (e.g., if we are investigating mindfulness techniques, then participants will be encouraged to engage in, or refrain from, mindfulness-related activities between [CBS](http://cambridgebrainsciences.com/) test measurements). Multiple regression will be used to estimate the contribution of each factors’ sub-features (e.g., duration, intensity, age of onset, etc.) to cognitive performance. Given our track record for collecting online datasets (7, 8, 23), we believe that we can generate massive and detailed population-level data about these factors, repeatedly and in a relatively short time frame. Our existing datasets will provide population-level norms against which we can compare these groups, and if required, can be used to generate samples matched on any of the variables that were included in our 50+ item questionnaire. Considering that the effects to be studied will be selected from the previous data-driven analysis, we expect to replicate those relationships, while further teasing apart the specific features that drive the relationship between that lifestyle or demographic variable and cognition.

**Impact**

Based on my lab’s recent track record, and on the nature and breadth of questions that will be answered by the research in this proposal, we will publish at least 5 papers in high-quality peer-reviewed journals each year. The results will be of interest to educators, policy makers, human resource professionals, psychologists, cognitive neuroscientists and anyone in the general population with an interest in how life-style factors and demographic variables *interact* to impact cognition. The results are also likely to attract significant media interest; indeed, our recently launched sleep and cognition study was covered on primetime BBC news in the UK, as well as by numerous radio and newspaper outlets *even before any data had been collected.* Our findings are also highly likely to pave the way for scientifically validated interventions and programs to help individuals optimize or improve their cognitive functioning. For example, we expect to gain a deep understanding of how factors such as sleep and physical exercise affect cognition and how they might be optimized to maximize life quality, including academic and work success. Finally, and perhaps most importantly, we believe that the approach to scientific enquiry that we outline in this proposal will provide a brand-new paradigm for future scientists to explore human cognition, whereby bottom-up data-driven discovery in the ‘real world’ leads to entirely novel hypotheses that can then be rigorously tested in the lab.

**Visual Abstract**

A diagram of a physical exercise and brain training

Description automatically generated

**Lay Summary**

Imagine only reaching out to people nearby versus thousands of people online? That is the power of the internet: expanding reach that is otherwise impossible—an advantage useful to science. This research project will use this advantage by organizing large-scale studies online to explore the link between demographic and lifestyle variables and the impact on cognitive performance. A testing platform will administer the online tests and the resulting databases will be used to examine the link. This research is made of three general parts. The first part investigates the relationship between sleep and cognitive function using a large database. We will observe the connection between duration and quality, varying levels of deprivation, and cognitive performance across age groups. In the second part we will look at how brain-training and physical exercise effect cognition, to understand a combination of both for the best brain functioning. The third part of the research aims to find subtle connections between lifestyle and demographic factors and the impact of other variables associated with cognitive performance. The power of the internet will allow us to gather high volumes of data, that otherwise we could not. Understanding how different lifestyle and demographic factors impact cognition at such a grand-scale can impact not only neuroscientists but countless other professions like educators, human-resource specialists, policymakers and more. Moreover, by using the internet to our advantage, we offer future scientist a new way, based on ‘real-world’ data, to investigate human cognition.

**Highly Qualified Personnel Training Statement**

The study will prioritize the training of 12 highly qualified personnel (HQP) into our interdisciplinary research team. Undergraduate and master student participation in our research projects is critical as it encourages students to pursue careers in research and provides clarity in specialized research subjects. Both master’s and undergraduate students will be mentored by PhD students. This training will introduce PhD candidates to mentoring. Principle investigators will be meeting with PhD students on a regular weekly basis to discuss the training progress and to guide PhD students in their mentorship role. Students will be delegated tasks that demonstrate their level of education and will be provided with training prior to completion. HQP’s will be provided with training on the following subjects, but not limited to data management, scientific writing, good clinical practice (GCP), safety reporting of adverse events, statistical analysis, regulation and ethical conduct. Ethical training will include equity, diversity and inclusion, as well as data privacy modules. New HQP’s will also be trained on the use of equipment such as the fMRI machines, as well as the Actiwatches, and will also be provided software training to be able to access different databases. These targeted training sessions will provide our HQP with the fundamental knowledge and skills for not only this study, but other future research endeavors too. HQP’s will be encouraged to join meetings regarding study details important in advancing the research. Opportunities to attend conferences will also be presented, and if HQP’s come across any alternate occasions for career growth and require our support, they are welcome to partake. Finally, we recognize the diversity in identity of every team member and ensure that each person is treated with dignity and respect, and condemn any form of discrimination, promoting a truly accepting environment for everyone.

**Sex and Gender Based Analysis**

Our team recognizes the presence of differences in sex and gender in research and with integrity, respect and inclusion will attempt to alleviate the impact through careful practices. During different parts of the study, we will be using different databases. When conducting the three different parts of the study there will be two analyses done for each part: sex based, and gender based. Therefore, when collecting data from WLSS or CBS databases, we will ensure to collect a similar quantity of data for the categories of female and male sexes to make relevant comparisons between the interactions of demographic and lifestyle variables and cognitive performance. Similar factors will be accounted for when conducting gender-based analyses, during collection of data for the demographic factor gender. Based on the different analyses we will conduct a comparative analysis on cognitive differences rooted in sex and gender. Further research will identify other variables, demographical, lifestyle, biological and/or more, that can be labelled as an underlying cause for the differences. Conducting sex and gender-based analyses in our study can lead to further research in the field of neuroscience regarding sex and/or gender-based differences in cognitive functioning.