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Association between physical activity and subjective memory decline triggered by the COVID-19 pandemic: Findings from the PAMPA cohort

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ABSTRACT

Implementation of social distancing reduced the incidence of coronavirus disease (COVID-19) cases. Nevertheless, this strategy has other undesirable effects such as physical inactivity and psychological distress, which are associated with cognitive impairment. We aimed to examine whether physical activity during social distancing restrictions could reduce the risk of subjective memory decline in adults. Participants (n=2321) completed the baseline assessment of PAMPA cohort (Prospective Study About Mental and Physical Health), a ambispective cohort study conducted in southern Brazil. An online-based, self-administered questionnaire assessed physical activity and self-rated memory in two different periods: before and during social distancing. Data collection was executed from June 22nd to July 23rd 2020. Adjusted Poisson regression models were performed and values reported in prevalence ratio (PR) with 95% confidence interval (CI). Participants presented with a mean age of 38.2 (95%CI: 37.5, 38.9) years. Most were women (76.6%), had at least a university degree (66.7%), and were overweight or obese (53.3%). Subjective memory decline was reported by 30.0% (95%CI: 27.7%, 32.4%) of inactive respondents. Physical activity participation during social distancing reduced the likelihood of subjective memory decline in adults. Physical activity should be highlighted as a potential alternative to reduce the burden of the COVID-19 pandemic on cognitive function and mental health.

1. Introduction

The novel coronavirus disease (COVID-19) has infected tens of millions and killed nearly 1,600,000 people worldwide since the first case was reported (Dong et al., 2020). This rapid spreading of the virus led governments to adopt restrictive measures such as social distancing (i.e., limiting physical interactions with others outside of their close family and leaving their homes only when necessary). Such a strategy is used to increase preparedness of healthcare systems and to mitigate the incidence of COVID-19 cases and related deaths (Islam et al., 2020; Nussbaumer-Streit et al., 2020). Notwithstanding its effectiveness, these approaches have been linked to unintended consequences such as psychological distress (United Nations, 2020; Pierce et al., 2020). Some recent studies have reported that social distancing increased the prevalence of depression and anxiety (Pierce et al., 2020), perceived stress (Stanton et al., 2020), sleep disorders (Casagrande et al., 2020; Huang and Zhao, 2020), and self-harm (Job et al., 2020).

An elevated burden on mental health might trigger an increase in memory complaints at the population level - another indirect consequence of the COVID-19 pandemic (United Nations, 2020). Previous studies have highlighted the association between psychological distress and subjective memory impairment (Bassett and Folsom, 1992; Smith

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Physical activity promotes several neuroprotective mechanisms, especially in the brain (Deslandes et al., 2009; Dishman et al., 2006; Erickson et al., 2019). Nevertheless, since the implementation of restrictions designed to prevent the spread of COVID-19, a reduction in physical activity levels has been documented in several settings (He et al., 2020; Lesser and Nienhuis, 2020; Smith et al., 2020), regardless of the degree of social distancing adopted (i.e., staying at home all the time, going out only for essential things, or going out every day to work or another regular activity). We have been reminded that the necessity of closing gyms and sporting clubs to prevent COVID-19 spread should not offset the importance of practicing physical activity during the pandemic (de Carvalho et al., 2020). Recent findings have demonstrated the beneficial role of physical activity during the pandemic on mental health (Pieh et al., 2020; Stanton et al., 2020). It would stand to reason a similar relationship may be observed for physical activity and subjective memory decline; however, to our knowledge no studies have evaluated the effect of social distancing restrictions on subjective or objectively-measured cognitive function in population-based samples. Therefore, we aimed 1) to determine whether subjective memory decline is a consequence of social distancing and 2) to evaluate the association between subjective memory decline and physical activity.

2. Methods

2.1. Study design

The study protocol was approved by the institutional research ethics board of the School of Physical Education of the Universidade Federal de Pelotas, Brazil (protocol: 4.093.170). The PAMPA cohort (Prospective Study About Mental and Physical Health) is characterized as an ambispective cohort study. Data on our primary outcome (i.e., subjective memory decline) and exposures were collected during COVID-19 social distancing to reflect two-time points: pre-COVID-19 social distancing and during COVID-19 social distancing. The period before social distancing was assessed retrospectively. More details about study design, sampling process, and data collection can be found elsewhere (Feter et al., 2020).

2.2. Sample

The inclusion criteria required participants to be an adult living in the Rio Grande do Sul state during the survey period. Sample size was calculated based on the prevalence of the three primary outcomes from this cohort (i.e. low back pain, mental health, and healthcare access). The highest sample size (N=1359) was achieved from depression prevalence (15.2%, 95%CI, 11.8%–15.0%) in the state of Rio Grande do Sul (Stopa et al., 2015), southern Brazil. Further, we accounted for a possible loss-to-follow-up of 30%. Therefore, our final sample size was estimated in 1767 adults living in the state of Rio Grande do Sul.

2.3. Participant recruitment

Full description of participant recruitment can be found in our previous publication (Feter et al., 2020). Briefly, we used local media (i.e., radio, TV, newspapers), professional colleagues, social media (i.e., Facebook® and Instagram®), and contact with city and state-level agencies of health to achieve the target sample size. The recruitment phase had a total duration of four weeks (June 22nd to July 23rd, 2020).

2.4. Questionnaire

We developed an online-based, self-administered questionnaire to evaluate the impact of the COVID-19 pandemic on memory and physical activity. Questions about self-rated memory and physical activity were asked twice to assess these outcomes based on different periods (before and during social distancing).

2.5. Primary outcome

2.5.1. Subjective memory decline

The instrument had two questions about self-rated memory. Participants were asked to rate their memory in the period before social distancing and present, using the following questions: “How do you rate your memory before social distancing?”, and “How do you rate your memory today?”. The options for both questions were “excellent”, “very good”, “good”, “fair” or “poor”. Subjective memory decline was defined as decreased memory perception. Similar questions have been used in previous epidemiological studies (Nunn et al., 2002; Vancampfort et al., 2017).

2.6. Exposure

2.6.1. Physical activity

We questioned participants about physical activity levels before and during social distancing. The first question was “Before social distancing, were you engaged in physical activity regularly?”. If the participant answered “yes”, then the total days and duration (minutes) of the activities during a typical week before that period were asked. The second question had the same format; however, the time-reference was the current week (during COVID-19 pandemic social distancing). This question presented a moderate agreement to classify subjects as physically active (kappa=0.63, 95%CI 0.54 to 0.72) compared to a longer questionnaire (e.g., Global Physical Activity Questionnaire) (Milton et al., 2011).

Respondents were stratified according to the World Health Organization’s guidelines for physical activity (World Health Organization, 2010). Adults aged 18–64 years complete 150 min or more of moderate-intensity aerobic physical activity throughout the week OR 75 min of vigorous-intensity aerobic physical activity or an equivalent combination were classified as physically active. Participants who did not achieve the guideline were classified as physically inactive. To explore the effects of changing physical activity on self-rated memory, we further classified participants based on physical activity classification in both periods, as follows: remained inactive, became inactive, became active, or remained active.

2.7. Possible confounding variables

2.7.1. Sociodemographic information

Questions on age, gender (male, female, other/prefer not to mention), ethnicity (white and non-white), conjugal status (with or with no partner), and the highest education level achieved were assessed.

2.7.2. Economic impact of COVID-19 pandemic

The impact of the social distancing in participants’ economic situation was evaluated. Participants were asked whether their monthly income was affected since the beginning of social distancing. When the answer was “yes”, they were requested to report whether their income increased or decreased.

2.7.3. Social distancing

Attitudes towards social distancing were asked by the following
question: “Regarding the social distancing that has been guided by health authorities, that is, staying home and avoiding contact with other people, how much of it do you think you are managing to do?”. The options available were “very little”, “little”, “somewhat”, “very much” and “totally isolated”. Participants were classified as “fully committed” with social distancing when answered “very much” or “totally isolated” to this question.

2.7.4. Chronic diseases
Self-reported weight, height, and whether there had been a clinical diagnosis of a chronic disease (e.g., hypertension, diabetes, depression) were asked using the same questions from the Brazilian Surveillance System of Risk Factors for Chronic Diseases by Telephone Interviews (VIGITEL) (Enes and Nucci, 2019). Weight and height were calculated to calculate the body mass index (BMI). Based on this value, the sample was categorized into the following groups: normal (\(\text{BMI} < 24.9\text{ kg/m}^2\)), overweight (25–29.9 kg/m\(^2\)), and obese (\(\geq 30\text{ kg/m}^2\)) (World Health Organization, 2018).

2.7.5. Aggravated depressive and anxiety symptoms
Mental health was assessed by the Hospital Anxiety and Depression Scale (HADS), which identified symptoms of depression and anxiety, both pre- and during social distancing. This 14-item scale was designed to provide a simple and reliable tool to be used in both community settings and primary care medical practice (Bjelland et al., 2002; Snaith, 2003). Each domain (depression and anxiety) has seven items that are scored between 0 and 3. Therefore, each domain has a maximum score of 21. Participants who scored less than 7 were classified as non-cases for that domain. Scores between 8 and 10 were considered as mild, between 11 and 14 as moderate, and between 15 and 21 as having severe symptoms of depression and/or anxiety (Zigmond and Snaith, 1983). Similar to physical activity, we compared the severity of symptoms between periods. Participants were classified with aggravated symptoms when they were classified in a worse severity group from before to during the COVID-19 pandemic.

2.8. Statistical analyses
Data were exported from Google® Sheets to Stata 13.1 (StataCorp, College Station, Texas). Due to a higher number of respondents from one region within the Rio Grande do Sul state (South, \(N=1247\) [53.7%]), all analyses were weighted for the number of respondents in each region. Continuous and categorical data were reported as mean and standard deviation (SD) or proportions and 95% confidence interval (CI), as appropriate. The chi-squared test was used to compare the difference in the proportion of participants among groups. Linear trend test was carried out to verify linear trend among groups. Independent t-test was used to verify difference in mean age between groups. The conceptual framework for our hypothesis is that depressive symptoms might lead to memory decline and reduced physical activity. Therefore, we first examined whether aggravated depressive symptoms had a mediation effect on the relationship between physical activity and subjective memory decline. Mediation effect was accepted if depressive symptoms had a significant association (\(p<0.05\)) with both outcome and exposure; then, the “kbb” test was ran, and when \(p>0.1\), mediation effect was accepted.

A multivariable Poisson regression was run to identify the impact of changing physical activity during the pandemic on subjective memory decline. The hierarchical model had two levels: In the first level, the sociodemographic variables (gender, age, ethnicity, educational attainment, conjugal status) were included in the model. In the second level, the variables related to the impact of social distancing on monthly income and mental health, commitment to social distancing, BMI, and diagnosed chronic diseases. Only variables with a p-value \(\leq 0.20\) were kept in the model. Alpha was set at 0.05 to indicate statistical significance of association between the independent variables with the outcome.

3. Results

Table 1 presents the sociodemographic and health-related characteristics of the final sample (\(N=2314\)). Participants reported a mean age of 38.2 (95%CI: 37.5%, 38.9%) years. Most were women (76.6% [95% CI: 74.4%, 78.7%]), white (90.6% [95%CI: 89.0%, 92.0%]), and had a university degree (66.7% [95%CI: 64.2%, 69.2%]),. Respondents reported a higher prevalence of overweight or obesity (53% [95%CI: 50.7%, 55.8%]), and chronic diseases (56.9% [95%CI: 54.3%, 59.3%]). Aggravated symptoms of depression affected roughly one third (35.0% [95%CI: 32.3%, 37.7%]) of our sample, while 51.3% (95%CI, 48.8%, 53.9%) revealed worse anxiety symptoms during social distancing.

We found a prevalence of subjective memory decline in 30.0% of the cohort (95%CI: 27.7%, 32.4%). This outcome was more frequently reported among younger adults, females, and those living without a partner. Further, they presented with a higher prevalence of chronic diseases, aggravated mental health, and acute economic strain since social distancing. Also, most individuals with subjective memory decline reported being physically inactive during social distancing. Indeed, the proportion of respondents who reported worse depressive and anxiety symptoms during social distancing were 2.1 and 1.9 times more common, respectively, in participants with subjective cognitive decline than in non-impaired ones. Although aggravated depressive symptoms were associated with both subjective memory decline (\(p<0.001\)) and reduced physical activity (\(p<0.001\)). No mediation effect was observed (\(p=0.828\)), suggesting a direct effect of physical activity on subjective cognitive decline.

Table 2 presents the Poisson regression models to examine the association between changes in physical activity behavior and subjective memory decline. Roughly one quarter (26.6% [95%CI: 24.4%, 28.9%]) of participants who meet physical activity guidelines (i.e., 150 min per week) before social distancing became physically inactive during this period. No noteworthy difference among models was noted, suggesting a consistency of the effect of physical activity on subjective memory decline. Adjusted analysis showed that participants who became inactive during the social distancing had the same probability (PR: 1.09; 95%CI: 0.88, 1.33) of reporting subjective memory decline than those who remained inactive behavior throughout the period. On the other hand, a sufficient level of physical activity reduced the likelihood of reporting this event. Participants who either became (PR: 0.56; 95%CI: 0.36, 0.89) or remained (PR: 0.68; 95%CI: 0.49, 0.93) physical activity during the COVID-19 pandemic were less likely to report a subjective memory decline. No remarkable changes were observed when adding socioeconomic variables (Table 2).

Fig. 1 illustrates the dose-response relationship between physical activity during social distancing and subjective memory decline. We observed a continuous decrease in the likelihood of subjective memory decline as the minutes per week spent on physical activity during social distancing increases.

4. Discussion
This study aimed to identify the effect of physical activity on subjective memory decline during social distancing. We found that roughly one third of adults from southern Brazil reported worse memory since the beginning of social distancing restrictions. Furthermore, remaining or becoming physically active during such restrictions reduced the probability of subjective memory decline even when analyses were adjusted for important confounding factors such as symptoms of depression and anxiety.

We observed that participants who reported subjective memory decline were female gender, had monthly income reduced, and aggravated symptoms of depression and anxiety since the beginning of social distancing. Alongside the rapid increase in the number of cases and
Table 1
Sociodemographic and health-related characteristics of included participants by presence of subjective memory decline. Rio Grande do Sul, Brazil. N=2314.

|          | Total  | Subjective memory decline | P-value |
|----------|--------|---------------------------|---------|
|          | (n=1621) | (n=692) |         |
| Age, years | 38.2 (37.5, 38.9) | 39.4 (38.6, 40.3) | 35.2 (34.1, 36.3) | <0.001¹ |
| Gender   |        |                           |         |
| Male     | 23.3 (21.3, 25.6) | 80.8 (76.2, 84.7) | 19.2 (15.3, 23.8) | <0.001² |
| Female   | 76.6 (74.4, 78.7) | 66.8 (63.9, 69.5) | 33.2 (30.5, 36.1) |         |
| Ethnicity |          |                           |         |
| White    | 90.6 (89.0, 92.0) | 70.0 (67.5, 72.4) | 30.0 (27.6, 32.5) |         |
| Non-white| 9.4 (8.0, 11.0) | 70.2 (62.3, 77.0) | 29.8 (22.9, 37.7) |         |
| Conjugal status | | | | |
| With partner | 61.6 (59.1, 64.1) | 72.3 (69.3, 75.2) | 27.7 (24.8, 30.7) |         |
| Living alone | 38.4 (35.9, 40.9) | 66.3 (62.3, 70.1) | 33.7 (29.9, 37.7) |         |
| Educational achievement | | | | |
| High school or below | 33.3 (30.9, 35.8) | 66.1 (61.8, 70.2) | 33.9 (29.8, 38.2) |         |
| University degree or above | 66.7 (64.2, 69.0) | 72.0 (69.1, 74.7) | 28.0 (25.3, 30.9) |         |
| Body mass index | | | | |
| Normal | 46.7 (44.1, 49.3) | 68.9 (65.4, 72.0) | 31.1 (27.7, 34.6) |         |
| Overweight or obese | 53.3 (50.7, 55.8) | 70.9 (67.6, 74.1) | 29.1 (25.9, 32.4) |         |
| Chronic disease | | | | |
| No | 43.1 (40.6, 45.7) | 72.1 (68.4, 75.4) | 27.9 (24.6, 31.6) |         |
| Yes | 56.9 (54.3, 59.3) | 68.5 (65.2, 71.6) | 31.5 (28.4, 34.8) |         |
| Fully committed with social distancing | | | | |
| No | 28.5 (26.3, 30.9) | 65.5 (60.8, 70.0) | 34.5 (30.0, 39.2) |         |
| Yes | 71.5 (69.1, 73.7) | 71.8 (69.0, 74.4) | 28.2 (25.5, 31.0) |         |
| Monthly income reduced since COVID-19 | | | | |
| No | 54.7 (52.2, 57.3) | 73.4 (70.3, 76.3) | 26.6 (23.7, 29.7) |         |
| Yes | 45.3 (42.7, 47.8) | 66.0 (62.2, 69.5) | 34.0 (30.4, 37.8) |         |
| Aggravated depressive symptoms since social distancing | | | | |
| No | 65.0 (62.3, 67.7) | 82.2 (80.4, 85.7) | 16.8 (14.3, 19.6) | <0.001³ |
| Yes | 35.0 (32.3, 37.7) | 59.2 (54.4, 63.8) | 40.8 (36.2, 45.6) | <0.001³ |

Table 1 (continued)

| Total  | Subjective memory decline | P-value |
|--------|---------------------------|---------|
| (n=1621) | (n=692) | |
| Aggravated anxiety symptoms since social distancing | | |
| No | 48.7 (46.1, 51.2) | 85.4 (82.6, 87.8) | 14.6 (12.2, 17.4) |         |
| Yes | 51.3 (48.8, 53.9) | 55.5 (51.9, 59.0) | 44.5 (41.0, 48.1) |         |
| Physical activity | | | | |
| Inactive | 74.5 (72.3, 76.7) | 66.5 (63.6, 69.2) | 33.5 (30.7, 36.3) | <0.001⁴ |
| Active | 25.5 (23.3, 27.8) | 80.2 (75.9, 83.9) | 19.8 (16.0, 24.1) |         |

¹ t-Test for independent sample [mean (95%CI)].
² Chi-square test (%) [95%CI] to compare the difference in the proportion of participants among groups.
³ Linear trend test.

Table 2
Changes in physical activity behavior and COVID-19-related subjective memory decline in adults in southern Brazil. Rio Grande do Sul, Brazil. N=2314.

| Change in PA | p-value Model 1 | p-value Model 2 | p-value Model 3 | p-value Model 3 |
|-------------|-----------------|-----------------|-----------------|----------------|
| Remained inactive (n=1016) | 1.00 | 1.00 | 1.00 | 0.005 |
| Become | 1.09 | 1.06 | 1.09 |         |
| inactive (n=626) | 1.29 | 1.27 | 1.33 |         |
| Become | 0.45 | 0.41 | 0.56 |         |
| active (n=172) | 0.29 | 0.26 | 0.36 |         |
| Remained | 0.87 | 0.67 | 0.68 |         |
| active (n=427) | 0.52 | 0.52 | 0.49 |         |
| Values are reported as prevalence ratio (PR) and 95% confidence interval (CI). Model 1: Crude analysis. Model 2: adjusted for gender, age, ethnicity, educational attainment, living alone or with a partner. Model 3: model 2 plus change in monthly income and mental health (i.e., depressive and anxiety symptoms) due to social distancing, commitments with social distancing, BMI, and diagnosed chronic diseases. |

Deaths, COVID-19 pandemic has led many countries to an acute economic strain(Fernandes, 2020). Constant concern about the future, combined with fake news(Cuan-Baltazar et al., 2020) and fear of contracting COVID-19(Fitzpatrick et al., 2020; Ornell et al., 2020) might impair mental health. Likewise, surveys on stress levels carried out in India(United Nations, 2020), China(Fu et al., 2020; Wang et al., 2020), and the United Kingdom(Pierce et al., 2020) during the pandemic indicated that women are at higher risk of psychological distress than men. Gender inequality in household activities led to a large burden of stress on women, who are commonly performing a double role, including managing their job and household-related activities(UNFPA, 2020). Also, people with chronic diseases are also considered at higher risk for more severe symptoms and mortality due to COVID-19(Baqui et al., 2020; Cummings et al., 2020; Jordan et al., 2020). The heightened stress of living with a chronic condition/s or having close friends or family with chronic conditions may increase the risk of psychological distress ultimately leading to memory complaints.

The United Nations highlighted the potential risk of the pandemic on...
cognitive decline in older adults, primarily driven by social isolation and physical inactivity (United Nations, 2020). However, our data revealed that the cognition of younger age groups can also be affected, which is in accordance with other studies ((Minds, 2020; Pieh et al., 2020; Pierce et al., 2020). A possible explanation for this may be due to a fear of losing the job, since young adults are less likely to be in an established position in their careers. Furthermore, some effects of the COVID-19 pandemic might be perceived only years after the end of social distancing. Thus, urgent action on groups at higher risk are required to prevent the long-term impact of this pandemic on both younger and older populations.

Despite the complexity of this relationship and the high prevalence of aggravated symptoms of depression and anxiety in our study, we found that physical activity had an important protective association with subjective memory impairment even after adjusting for such symptoms. Indeed, we observed that using different models with adjusted analyses did not affect the strength of this association. Worse depressive and anxiety symptoms during social distancing restrictions were 2.1 and 1.9 times more common, respectively, among respondents with subjective memory decline than in non-impaired participants.

Physical activity is a powerful non-pharmacological strategy to reduce the risk of depression and anxiety during the COVID-19 pandemic (Pieh et al., 2020; Stanton et al., 2020; Zhang et al., 2020). This protective effect may be associated with increased availability of neurotransmitters (Jovanovic et al., 2000) and neurotrophic factors (Feter et al., 2019) which are well-known promoters of neurogenesis (Deslandes et al., 2009; Vivar et al., 2013), angiogenesis (Duggan et al., 2016; Duggan et al., 2014; Newton and Duman, 2004), and synaptic plasticity (Vaynman et al., 2004; Vivar et al., 2013). Altogether, these neuroprotective mechanisms induce enhancements in cognitive performance in healthy (Cotman and Berchtold, 2002; Dishman et al., 2006) and clinical populations such as adults with mild cognitive impairment (Gates et al., 2013) and dementia (Heyn et al., 2004). Reduced stress levels have been found to mediate the association between increased physical activity and reductions in subjective memory impairment (Phillips et al., 2017). However, our findings indicate that the protective effect of physical activity on memory decline is not mediated by aggravated depressive symptoms. As face-to-face interactions between participants and trainers are not recommended during social distancing, internet or telephone-based programs to promote physical activity should be encouraged to alleviate the effect of the COVID-19 pandemic on self-perceived cognitive function.

Notwithstanding the relevance and novelty of our findings, some limitations of the present study must be acknowledged. First, the retrospective design for questions about mental health and physical activity before and during social distancing might have some degree of recall bias. Although the recall bias cannot be ruled out, the COVID-19 pandemic is such an unprecedented event in everyone’s life that it can help people to clearly remember their health habits or issues, such as low back pain or physical activity practice, for example, thus reducing the risk of recall bias. Second, as face-to-face interviews were not allowed by the local ethics board, questionnaires were self-administered. Therefore, response bias may be a limitation. Third, the use of self-rated memory could underestimate the negative impact of social distancing in cognitive function (Jungwirth et al., 2004). Nevertheless, objective measurements of cognitive function were not possible due to such restrictions. Lastly, the proportion of participants self-declared white (90.6% [95%CI, 89.0% to 92.0%]) and aged 30 years or over (62.7% [95%CI, 60.2% to 65.2%]) is similar to the general population of the Rio Grande do Sul state (whites: 79%; adults aged 30 or over: 62.2%). Nevertheless, respondents with one or more academic degree is overrepresented in our sample. Data from the latest Continuous National Household Sample Survey (Continuous PNAD) (IBGE, 2020) revealed that 16.9% of adults aged 25 years or more had at least one academic degree, while in our sample, this proportion was 40.2% (95%CI, 37.8% to 42.8%). This sampling bias was expected, since data collection was online and poorer/less educated individuals have less access to the internet compared to richer/more educated people in Brazil. However, COVID-19 is likely to have had a larger impact on the lower economic groups of the population, thus our results are likely underestimated. Had our sample included a higher proportion of less educated individuals, an even higher prevalence of subjective cognitive decline may have been observed.

5. Conclusion

We conclude that subjective memory decline affected one in every three adults in southern Brazil following the beginning of social distancing. However, remaining or becoming physically active during such restrictions reduces the likelihood of this impairment. Studies with objective measurement of different domains of cognition are required to better understand the effect of the COVID-19 pandemic on cognitive function at the population level.

Statement of authors contributions

NF, ELC, IGR, FFR, MCS, and AJR conceived the study. NF performed all analyses and led the writing of the manuscript. JSL, JC, ECS, JSC, FFR, MCS, and AJR revised manuscript. All authors approved the final version of the manuscript.

Declaration of Competing Interest

None.

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