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Longitudinal Study of Cognitive Decline before and after the COVID-19 Pandemic: Evidence from the PA-COVID Survey

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Coronavirus disease 2019 · Pandemic · Older adults · Cognitive decline · Mental health

Abstract
Introduction: Even though several studies reported good resilience capacities in older adults in the first period of the coronavirus disease 2019 (COVID-19) pandemic, in the long run, social isolation induced by the protective measures adopted by most countries may negatively impact cognitive functioning. Taking the advantage of measures collected up to 15 years before the pandemic in participants followed up in epidemiological studies, we compared cognitive decline before and after the start of the pandemic. ***Methods:*** PA-COVID is a phone survey designed in the framework of ongoing population-based studies (PAQUID, 3-City, Approche Multidisciplinaire Intégrée cohorts). Data on social functioning and mental health were collected in participants aged 80 years and older during the pandemic. Prior to the pandemic, the participants followed up in the prospective studies completed the Mini-Mental State Examination. During the PA-COVID survey, they underwent the Telephone Interview for Cognitive Status. A score was computed with the 11 items shared by the 2 tests. Our analysis was carried out in the participants for whom a cognitive measure was available up to 15 years before the pandemic and during the pandemic (n = 263). ***Results:*** Compared to the slow decline of the cognitive subscore observed during the 15 years preceding the pandemic, mixed models showed an acceleration of decline after the start of the pandemic ($\beta = -0.289$, p value <0.001). ***Conclusions:*** With a design allowing comparing cognitive trajectory before and after the pandemic, this is the first study reporting an accelerated decline in older adults. Future COVID research in older adults will need to pay special attention to cognitive outcomes.

Introduction

Many physical and functional specificities make the elderly population particularly vulnerable to the coronavirus disease 2019 (COVID-19) pandemic. Even though several studies reported good resilience capacities of older adults with relatively low levels of anxiety and depression in the first period of the pandemic [1–6], in the long run, the protective measures adopted by most countries

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to fight against the pandemic could have an impact on cognitive functioning. Indeed, the reduction of social contacts including with close relatives, and the physical distancing, along with the imposed lockdown periods induce both qualitative and quantitative substantial changes in older adults' lifestyle that may be potentially harmful and lead to further cognitive decline, as we know that social isolation in older persons strongly affects health-related outcomes [7].

In older adults suffering from cognitive impairment and/or neurodegenerative disorders, few studies support this hypothesis. For instance, Gan et al. [8] reported in 205 patients with cognitive impairment or Alzheimer's disease, a greater decline in several cognitive scales assessed during the pandemic compared with a control group which was assessed before the pandemic. This result is consistent with the study by Tsapanou et al. [9] conducted among 204 family caregivers of older adults with mild cognitive impairment or dementia who reported a significant overall decline in the patients. Other studies in smaller groups of patients [10] or in nursing home residents [11] also support these findings.

However, if a small number of studies are available in people with cognitive impairment or dementia, much scarcer are those that focused on older adults in the general population. Of those, the study by Ingram et al. [12] was based on 342 participants aged 18–72 years followed up for 13 weeks during the pandemic with repeated measures collected with online cognitive tests. The results showed that social isolation was associated with greater decline in cognitive performances. However, the study included not only some older adults but also younger age categories. In addition, no measure prior to the pandemic was available. Noguchi et al. [13] conducted a survey among 955 older adults living in the community in Japan who were required to answer a questionnaire by postal mail. In this study, social isolation was associated with a self-reported decline in cognitive function. Unfortunately, no objective measure was available, so it may be difficult to know whether such a self-perceived decline reported by the respondents is the result of a real worsening of cognitive function or rather reflects the fear of decline generated by the anxiety induced by the context. Mixed results were reported in another study relying on an online survey in almost 600 older adults living in Belgium [14]. The authors found that the COVID-19 pandemic had a severe impact on the well-being, activity level, and sleep, while only a small group of participants (those with depressive symptoms) reported a decline in cognitive functioning. However, as underlined by the authors themselves, due to the procedure of recruitment (Internet-based survey), the study sample is rather homogenous as most participants were in good health, were cognitively able to answer online, and had a high socioeconomic status, as shown by their level of education and income. In addition, cognitive function was assessed with questions on self-perceived change.

Obviously, we lack studies allowing proper quantification of the impact on cognition of the disruption in older adults' daily life due to the pandemic context. Such studies are difficult to set up. Indeed, to evidence a change in cognitive function, which is supposed to change with age, we need longitudinal studies that measured cognitive outcomes in older adults not only during the pandemic but also several years before the pandemic in order to compare the rate of change in cognition and identify a potential breakpoint in the trajectory.

The present work is part of the PA-COVID study, a phone survey conducted among older adult participants during the pandemic, designed in the framework of already existing prospective population-based studies. The study aims at investigating the impact of the COVID-19 pandemic on cognitive decline in older adults. To do this, we took the advantage of the available cognitive measures collected up to 15 years before the pandemic in the participants to compare the trajectory of cognitive decline before and after the start of the pandemic.

Methods

Study Population

The PA-COVID survey was built in the framework of 3 ongoing epidemiological studies on ageing: PAQUID (Personnes Agées QUID), Bordeaux sample of the 3-City (the Bordeaux sample is the one with the most thorough follow-up in particular for cognitive outcomes), and AMI (Approche Multidisciplinaire Intégrée) cohorts [6]. Briefly, the PAQUID study is an epidemiological survey relying on a population-based sample of 3,777 community-dwelling individuals aged 65 years or older randomly selected from electoral rolls [15]. Participants were followed up since 1988 until 2019. The 3-City was conducted in 3 French cities (Bordeaux, Dijon, and Montpellier) [16]. For the PA-COVID survey, only the Bordeaux sample initially consisting of 2,104 community-dwelling individuals aged 65 years or older randomly selected from electoral rolls, enrolled between 1999 and 2001, and followed up until 2017 was considered. Finally, AMI is an epidemiological study conducted to study the specificities of ageing in rural communities [17]. The initial sample included 1,002 retired farmers aged 65 years and older, randomly selected from the Farmer Health Insurance System. They were followed up between 2007 and 2019. The cohort studies rely on a similar design. The participants were visited at home approximately every 2–3 years by a trained psychologist who administered various scales and questionnaires assessing

physical, social, and mental health. The clinical diagnosis of dementia was made following a 3-step procedure: (1) a cognitive evaluation made by the psychologist with a series of psychometric tests, (2) the participants who had a high likelihood of presenting dementia based on their neuropsychological and functional performances were examined by a neurologist or geriatrician, (3) each case was discussed by a validation committee composed of senior neurologists and geriatricians to provide a consensual diagnosis.

Conducted within these cohorts, the PA-COVID survey was designed to assess the psychological and social impact of the COVID-19 pandemic in people aged 80 years and older, still alive and followed up in the framework of the cohort studies. Participants were contacted by phone by psychologists to offer to participate in the PA-COVID survey. The phone interview lasted about 40 min and included several questions on different dimensions: living conditions during the lockdown, coping strategies, mental health (anxiety and depressive symptoms), cognitive function, subjective health status, functional status, social support (objective and subjective), knowledge about the pandemic, and the protection measures recommendations. A first wave was conducted during the first lockdown in France (March–June 2020) and the second wave, 2–3 months later (July–September 2020).

For the present study aiming at investigating cognitive decline before and after the start of the pandemic, the 5 follow-up visits preceding the PA-COVID survey were considered. Participants with more than 1 missing visit among the 5 visits preceding the pandemic were excluded.

Matching AMI and 3-City follow-up visits was possible since they were done at about the same time and each visit was separated by an interval of 2–3 years. The baseline visit of the AMI cohort and the 4-year follow-up visit of the 3-City study are visit 1 in the present study. Subsequent visits of AMI and 3-City studies are visits 2–5 for the present study. Finally, visit 6 corresponds to the PA-COVID survey. None of the participants gathered from the PAQUID study could be included in the present analysis (see the next section on the selection of participants).

Cognitive Function Measure

In 3-City and AMI studies, various cognitive tests are repeatedly administered to assess cognitive functioning. Among these tests, the Mini-Mental State Examination (MMSE) test [18] was administered at each follow-up and in both cohorts. This widely used test consists of 30 items and involves questions assessing orientation to space and time, memory, calculation, visuoconstruction, and language skills.

Cognitive function was also measured during the second wave of the PA-COVID survey. As the MMSE test could not be administered by phone, the French version of the Telephone Interview for Cognitive Status (TICS) was proposed [19]. The TICS consists of 43 items, including items assessing orientation to space and time, episodic and semantic memory, calculation, and language skills. The total score can range from 0 to 43 (the lower the score, the weaker the performance). The TICS has been validated for phone administration and has shown a very high correlation with MMSE [20]. Indeed, the MMSE and TICS tests have some commonalities. Unlike other tests that assess a specific cognitive function (e.g., episodic memory, language, executive functions), both tests were designed to assess global cognitive function. More importantly, several items are identical. Therefore, in order to study the evolution of a marker of cognitive functioning assessed before and after the start of the pandemic, we built a score composed of the 11 items shared by the 2 tests. The 11 common items are the following: (1) What is the day of the week? (2) What is today's date? (3) What month is it? (4) What year is it? (5) What city are we in? (6)–(10) Subtract 7 from 100 and so on? (11) Repeat "no, ifs, ands or buts."

Statistical Analyses

First, the study sample was described according to socio-demographic variables such as age, sex, level of education, the presence of a dementia diagnosis, and the total TICS score at visit 5. The quantitative variables (age and TICS score) were described according to their mean and standard deviation. For the qualitative variables (sex, education level, and dementia diagnosis), the number and percentage of participants in each modality were reported.

In order to investigate the presence of a potential accelerated cognitive decline after the start of the pandemic, a latent process mixed-effects model was conducted. The latent process mixed model is a mixed model allowing correction of the non-Gaussian longitudinal cognitive subscore distribution. The latter was transformed to correct the departure from normality using parameterized link functions [21]. The optimal link function, quadratic I-splines with three knots, was selected according to the Akaike information criterion.

Mixed models allow analysis of longitudinal data and testing a significant change in the slope. For this, a time-dependent indicator variable is used to indicate when the slope change occurs, being 0 for the visits prior to the pandemic and 1 for the visit during the pandemic (PA-COVID survey). The within-participant correlation was captured by random intercept and slope on time. The models were adjusted for age. A potential cohort effect on the slope of decline was also statistically assessed by the model. All statistical analyses were performed with the RStudio software version 4.0.3 [22].

Results

Selection of Participants

The PA-COVID survey included 467 older adults. Of these, 248 participants were gathered from the 3-City study, 162 participants from the AMI study, and 47 from the PAQUID study. Of the PAQUID participants interviewed, none had a complete TICS test. Indeed, the PAQUID study is a very long-lasting study (started in 1990), so the few still alive participants are 95 years and older, explaining the higher propensity to refuse cognitive testing due to fatigue or hearing loss. Of the participants of the 3-City and AMI studies, 132 were excluded because the TICS was not complete and 15 were excluded because they had more than 1 follow-up visit missing prior to PA-COVID. Therefore, the study sample consisted of 263 participants.

Study Sample Description

Table 1 displays the characteristics of the participants considered for the present study. The mean age of the

Table 1. Description of the characteristics of the study sample (*n* = 263): results from the PA-COVID survey

Characteristic	3C (*n* = 148)		AMI (*n* = 115)		Total (*n* = 263)	
	n/mean	%/SD	*n*/mean	%/SD	*n*/mean	%/SD
Age (mean, SD), years	91.1	3.0	84.7	4.5	88.3	4.9
Sex	148		115		263	
Men, *n* (%)	47	31.8	61	53.0	108	41.1
Women, *n* (%)	101	68.2	54	47.0	155	58.9
Education level	148		115		263	
No schooling, *n* (%)	8	5.4	24	20.9	32	12.2
Primary school validated, *n* (%)	27	18.2	47	40.9	74	28.1
Short secondary school validated, *n* (%)	43	29.1	34	29.6	77	29.3
Long secondary school validated, *n* (%)	32	21.6	5	4.3	37	14.1
Higher education, *n* (%)	38	25.7	5	4.3	43	16.3
Dementia	148		115		263	
Yes, *n* (%)	2	1.4	0	0.0	2	0.8
No, *n* (%)	146	98.6	115	100.0	261	99.2
TICS score (mean, SD)	27.8	6.9	29.3	5.7	28.4	6.4

SD, standard deviation.

Table 2. Comparison of the participants included in the study and those excluded (because of missing data in the TICS test or missing previous follow-up visits): results from the PA-COVID survey

Characteristic	Included participants (*n* = 263)		Excluded participants (*n* = 147)		*p* value
	n/mean	%/SD	*n*/mean	%/SD	
Age (mean, SD), years	88.3	4.9	89.9	4.5	<0.001
Sex	263		147		0.09
Men, *n* (%)	108	41.1	47	31.9	
Women, *n* (%)	155	58.9	100	68.1	
Education level	263		147		<0.01
No schooling, *n* (%)	32	12.2	37	25.2	
Primary school validated, *n* (%)	74	28.1	31	21.1	
Short secondary school validated, *n* (%)	77	29.3	32	21.8	
Long secondary school validated, *n* (%)	37	14.1	23	15.6	
Higher education, *n* (%)	43	16.3	24	16.3	

SD, standard deviation.

participants coming from the 3-City cohort was higher than that of the participants coming from the AMI cohort (91.1 vs. 84.7 years), with an average age for the whole sample of 88.3 years (SD = 4.9). The sample gathered from the 3-City included more women than men, while the AMI cohort included almost as many men as women. In the whole study sample, there were slightly more women than men (155 vs. 108). Regarding education level, among the participants from the 3-City cohort, the most frequent education level was short secondary school. In participants from the AMI cohort, the level of education was slightly lower, with the validated primary certificate being the most represented category. Two participants of the 3-City study had a diagnosis of dementia before the PA-COVID survey. Finally, the mean TICS score in the 3-City participants was 27.8 (SD = 6.9) and 29.3 (SD = 5.7) in AMI participants, while the mean score for the whole study sample was 28.4 (SD = 6.4). As can be seen in Table 2, compared to the participants excluded from the analysis, the included participants were younger (mean age 88.3 vs. 89.9 years) and were slightly higher educated. There was no difference in sex proportion.

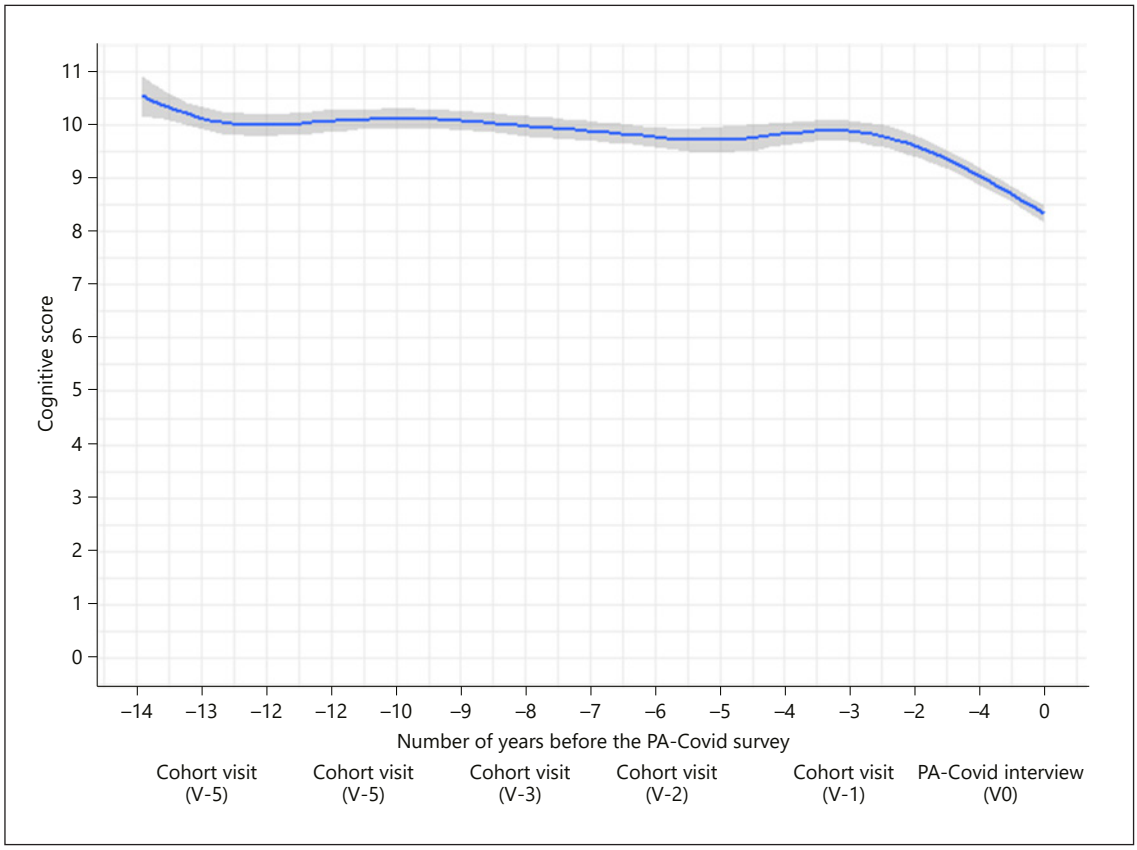

Fig. 1. Evolution of the 11-item TICS/MMSE score obtained at previous cohort follow-up visits up to the PA-COVID survey: results from the PA-COVID survey (n = 263).

Figure 1 displays the curve of cognitive score evolution all along the follow-up period considered, including the PA-COVID follow-up and the 5 preceding visits. The figure shows an acceleration of decline concomitant to the pandemic.

Results of the Mixed Models

Table 3 presents the results of the mixed model adjusted for age. The results show a small but non-significant decline in the cognitive score before the start of the pandemic (p value = 0.387). When considering the pandemic time in the follow-up, a negative and significant interaction is found (p value <0.001), which means that after the start of the pandemic, the decline is significantly greater (β = −0.289; SD = 0.032). The model assessed a potential age effect; the objective was to assess whether the decline was different depending on the age of the participants. The results show that the interaction between time and age is not significant (p value = 0.614), meaning that age has no effect on the rate of cognitive decline.

Table 3. Results of the linear model with mixed effects conducted on the available data modelling the evolution of the 11-item TICS/MMSE score before and after the start of the pandemic: results from the PA-COVID survey (n = 263)

	β	S (β)	p value
Time	−0.093	0.107	0.387
Time-dependent indicator	2.928	0.346	<0.001
Age	−0.032	0.012	0.010
Time × time-dependent indicator	−0.289	0.031	<0.001
Time × age	<0.001	0.001	0.613

The model also assessed the potential cohort effect. Indeed, it was important to ensure that the results observed are not specific to one of the cohort studies but are similar in the 2 populations. As can be seen, the interaction between time and cohort is not significant (p value = 0.835), which means that the cohort has no effect on the rate of cognitive decline.

Discussion

In the present study, we examined the cognitive change in older adults due to the COVID-19 crisis in a sample of French older persons living in the community. Compared to the slow and non-significant decline in the cognitive subscore all along the almost 15 years preceding the pandemic, we found that the rate of decline about 5–6 months after the start of the pandemic is far greater, with the change in the slope of decline being highly significant. This finding is consistent with what could be extrapolated from the very scarce studies available [12, 13]. However, this is the first study that reports such a striking finding based on a design allowing comparison of the trajectory of decline before and after the pandemic.

With the current pandemic, individuals undergo lifestyle changes that threaten to disrupt the social functioning and daily routines that are essential to promote mental health, especially [23] in older adults [24]. Such abrupt changes in daily and social activities, which persist over time, may negatively impact cognitive functioning and can potentially lead to future cognitive decline. To some extent, a parallel can be drawn with the effects of occupational retirement on cognition, the drastic changes in daily and social life due to retirement from work being assumed to underlie such a negative impact on older adults' cognitive functioning [25].

The main limitation of this study lies in the measure of cognitive functioning. Indeed, due to the barrier measures, we could not visit the older participants at home to assess cognition, as we did in the previous follow-up visits of the cohorts. The MMSE collected during the previous assessment visits required a face-to-face interview, which was not possible during the pandemic. Consequently, it was not possible to use the same complete scale of cognitive performance. However, both MMSE and TICS were designed to assess cognitive function globally, and they show a high correlation [20]. In addition, the score considered for this study consists of the 11 items the 2 tests have in common, which are strictly identical. Although the range of cognitive functions assessed is limited, the score covers orientation to time and space, working memory, and language. In addition, orientation to time items of the MMSE have been shown to be highly correlated to episodic memory [26]. However, it is important to underline that this limitation calls for future research to confirm our results.

Despite this limitation, our study has several strengths: the first being the 15 years of follow-up available prior the PA-COVID survey. To our knowledge, this is the first study that reports an acceleration of cognitive decline based on a design comparing the same cognitive measure collected during the pandemic with the trajectory of decline before the pandemic. Moreover, given the obvious time constraints, many research studies on the consequences of the pandemic have been based on online surveys inducing important selection bias of participants, as volunteers in such studies are generally older adults in good health and with a rather high socio-economic status [27]. Based on phone interviews and on participants who were already enrolled in different ongoing cohorts and come from diverse settings, the study sample results in a diversified panel of participants, limiting the selection biases. Indeed, the study sample involves a good balance between men and women, rural and urban population, low- and high-educated individuals, and includes oldest old participants (aged 80 years and older). Also, phone interviews were conducted by trained psychologists with extensive experience in geriatrics and cognitive assessment in older adults.

Conclusion

Older adults were identified as a group at risk due to the high mortality associated with COVID-19 infection. Nonetheless, they should be seen as a group at risk with regard to cognitive health issues also. Whether the observed cognitive decline is just temporary reaction to the crisis, whether the evolution will be reversed in the next months/years, or whether it will continue to worsen with the still ongoing pandemic is an issue with obvious public health and clinical implications. The currently ongoing follow-up of the PA-COVID survey may provide some clues. More generally, future COVID research in older adults will imperatively need to pay very special attention to cognitive outcomes.

Statement of Ethics

For the 3-City cohort, the study protocol was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre, and participants signed the informed consent (project number N 99-28). PAQUID (authorization number CNIL 998-249) and AMI (registration number 2006-A00595-46) studies received approval from the Ethics Committee of the Bordeaux University Hospital according to the principles embodied in the Declaration of Helsinki. The patients/participants provided their written informed consent to participate in this study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

H. Amieva designed the PA-COVID study, supervised the data analysis, and wrote the manuscript. N. Retuerto and C. Meillon performed statistical analyses and revised the manuscript. J.F. Dartigues, V. Hernandez-Ruiz, and K. Pérès revised the manuscript.

Data Availability Statement

The datasets for the cohorts presented in this article are not readily available as they are the property of the Université de Bordeaux. Requests to access the datasets should be directed to helene.amieva@u-bordeaux.fr.

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