Do I Lose Cognitive Function as Fast as my Twin Partner? Analyses Based on Classes of MMSE Trajectories of Twins Aged 80 and older

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Research article

Keywords: Twins, Growth Mixture Models, Cognitive trajectories

Posted Date: February 4th, 2020

DOI: https://doi.org/10.21203/rs.2.22580/v1

Version of Record: A version of this preprint was published at Age and Ageing on October 31st, 2020. See the published version at https://doi.org/10.1093/ageing/afaa239.

Abstract

Background: Aging is associated with an increasing risk of decline in cognitive abilities. The decline is, however, not a homogeneous process. There are substantial differences across individuals although previous investigations have identified individuals with distinct cognitive trajectories. Evidence is accumulating that lifestyle contributes significantly to the classification of individuals into various clusters. How and whether genetically related individuals, like twins, change in a more similar manner is yet not fully understood.

Methods: In this study, we fitted growth mixture models to Mini Mental State Exam scores (MMSE) from participants of the Swedish OCTO Twin study of oldest old monozygotic (MZ) and same-sex dizygotic (DZ) twins with the purpose of investigating whether twin pairs can be assigned to the same class of cognitive change.

Results: We identified 4 distinct groups (latent classes) whose MMSE trajectories followed various patterns of change over time: a class of stable and high performing individuals, two groups of high performers who declined at different annual rates, and a small group of impaired individuals who declined more rapidly. Notably, our analyses show that few individuals in fact could be assigned to the same class as their co-twin.

Conclusions: Our study provides evidence for more substantial impact of environmental, rather than genetic, influences on cognitive change trajectories in later life.

Introduction

Twins provide a unique and valuable source of information to better estimate the relative importance of genetic and environmental influences on various traits and functions. However, it is becoming increasingly apparent that the genetic setup can account only for a portion of the observed variance in most processes related to development, function, and disease. Monozygotic twin pairs (MZ), despite sharing identical DNA sequences, are often discordant, indicating that the same genotype in fact can produce distinct phenotypes. This points towards the involvement of environmental influences and gene-environmental (GxE) interactions. It is therefore quite unlikely that the unique sequence of our genomes provides the full blueprint for observed traits and functioning.

Cognitive health and functioning are domains shown to be influenced by genetics as well as modifiable environmental risk factors. Twin studies converge on the conclusion that cognitive abilities are quite heritable also in later life (e.g. McGue and Christensen (1); McClearn et al. (2) using baseline data from the sample in the present). There are, however, differences related to specific ability under study. Analyses of subgroups defined by their actual cognitive level can present a more differential picture. For example, analyses by Petrill et al. (3), using baseline data from the sample used in the present study, showed high heritability for the high end of the distribution, but very low heritability at the low performance continuum. Longitudinal studies have shown that the E4 variant of the Apolipoprotein E allele is associated with

greater cognitive decline among individuals without dementia (4). There is also a substantially increased risk among E4 variant carriers, especially in those with two ε4 alleles, to develop dementia (5). Although the E4 allele is known as the single most influential genetic risk factor for late-onset sporadic Alzheimer's disease (AD), it cannot be considered as the determinant of the disease.

Many studies have shown that healthy lifestyle behaviors have a protective role. Individuals who engage in these behaviors typically perform better on cognitive tests and decline at a slower rate than those with a less healthy lifestyle. For instance, nonsmokers have been shown to decline at a slower rate in specific and global cognitive functions compared with smokers (6, 7). Similarly, it has been shown that individuals who engage in cognitively stimulating activities decline at a slower rate than individuals who do not stimulate their brains (8-10). They also have a lower risk of subsequent cognitive impairment and dementia (10-13). Furthermore, individuals with a physically active lifestyle decline at a slower rate than more sedentary individuals (14, 15). Existing evidence has examined the role of many modifiable risk factors on cognitive trajectories in older adults. But, these studies have often neglected the heterogeneity which is likely to produce subgroups of individuals with distinct cognitive trajectories (classes). The question is whether a classification of individuals into different subgroups, defined by their exposures to potential risk factors, can inform us about the relative contribution of environmental and underlying genetic influences.

A first step toward an improved understanding of the observed heterogeneity of cognitive change is to cluster individuals according to their trajectories over time and then to identify distinguishing factors that contribute to the classification of individuals into clusters. Growth mixture models, GMM (16), offer analytical models specifically developed to identify groups of individuals (latent classes) who change in a similar manner. A multinomial logistic model with covariates can also produce a probabilistic classification of individuals into each of the classes identified.

Several studies have employed this methodology to improve knowledge about aging related cognitive decline. For example, Muniz Terrera, Matthews , and Brayne (17) fitted GMM to Mini Mental State Exam scores (18) from a British sample aged 75 years and older at study entry. They identified a group of individuals whose Mini-Mental-State-Examination (MMSE) scores remained stable over time, another group that declined at fast rate and a third group of medium rate decliners. Olaya, Bobak, Haro, and Demakakos (19) analysed episodic memory scores from participants of the English Longitudinal Study of Ageing and identified 4 groups of individuals (low/decline, low/stable, average/stable and good/stable group) in the sample of individuals who entered the study aged 59-64 years old; whilst in the group of older adults (65-79 years at study entry), they identified 4 groups characterized as very low/rapid decline, low/decline, average/stable and good/stable. Hayden et al. (20), in an analysis of a global composite cognitive score, derived from a battery of 19 neuropsychological tests administered in the Religious Order Study, identified 3 groups; individuals whose trajectories over time were characterized with slow decline from a slightly above average baseline score, a group of moderate decliners, and a third group of individuals whose baseline score were low followed by a fast decline. The literature provides increasing evidence demonstrating a great heterogeneity of cognitive trajectories in older adults. However, research

efforts focusing specifically on heterogeneity in the segment of the oldest old is limited. In addition, we lack knowledge about whether pairs of twins in this segment of the population show similar trajectories.

In this paper, we used data from the OCTO Twin Study, a longitudinal study of Swedish twins aged 80 and older, to examine whether: *(i)* we can identify distinct classes or clusters of individuals with similar cognitive trajectories, defined by their scores on the Mini Mental State Exam (MMSE), *(ii)* pairs of monozygotic twins (MZ) are more likely than pairs of same-sex dizygotic twins (DZ) to be assigned to the same class, and (*iii*) a list of a set of previously identified and modifiable risk factors are relevant for the assignment of individuals into various classes.

Analytical Methods

OCTO Twin Study

The sample used in these analyses was drawn from the comprehensive longitudinal Origins of Variance in the Old-Old: Octogenarian Twins (known as the OCTO-Twin Study) based on the oldest cohort of the Swedish Twin Registry (21). The sample includes 702 participants, with 351 complete twin pairs (149 identical (monozygotic) and 202 same-sex fraternal (dizygotic pairs)), born in 1913 and earlier, who were, or became, 80 years of age during the first wave of data collection (1991-1993). Participants were re-assessed biannually (over an 8 year period) at their homes or place of residency by medical research nurses specially trained for the study. The average rate of attrition from one wave of examination to the next was 20% (10% per year), primarily due to death. Full details of the study population characteristics have been published previously (2, 21, 22), including findings on cognitive performances relative to survival (see Johansson et al. (23)).

Global cognitive function was assessed using the Mini-Mental State Examination MMSE screening device (18), which has become a frequently used screening device for overall cognitive function in clinical and research samples. The MMSE measures various domains including orientation, registration (immediate memory), short-term memory (but not long-term memory), attention, the ability to follow verbal and written commands, writing and copying. Scores range from 0–30 and high values indicate better cognitive status. The observed trajectories and scores in our sample, plotted against years past from baseline, are depicted in Figure 1.

In addition to socio demographic information about participants such as age, sex and years of education, whether or not they ever received a dementia diagnosis, lifestyle information was also collected. Specifically, smoking habits were assessed by asking whether participants ever smoked, they smoked “now and then”, they had been smokers but quitted or whether they were current smokers. Participants were also asked about whether they had or presently stimulated their brains to some or a large extent in cognitively demanding activities. They were also asked whether they trained and stimulated their bodies to some or a large extent. Table 1 presents the descriptive characteristics of the sample.

Ethics

The OCTO-Twin Study received approval from the Ethics Committee at the Karolinska Institute in Stockholm and from the Swedish Data Inspection Authority. Informed written consent was obtained from all participants or their relative or caregiver where capacity to consent was questionable, for example, due to severe cognitive impairment or dementia.

Statistical Analysis

We fitted a series of growth mixture models (GMM) to MMSE scores aligned as a function of number of years past from study entry to identify subgroups (classes) of individuals with similar MMSE trajectories. The number of available time points (i.e. 5 waves) allowed us to examine linear as well as accelerating patterns of change. Class specific intercepts and slopes were adjusted for sociodemographic factors (age, sex and education) and a dementia indicator variable. To learn about the role of these sociodemographic factors and of lifestyle factors on class assignment, we adjusted the multinomial logistic model for class probability for baseline age, education, sex, smoking status, physical activity and engagement in cognitively stimulating activities.

Baseline age and education (measured in years) were modelled as continuous variables centered at the sample median values, 83 years of age and 7 years of education respectively. A dementia indicator was coded as 1 if an individual ever received a diagnosis of dementia and 0 if the individual never was diagnosed with dementia during the study period. Sex was coded as 0 for a male participant and 1 for a female participant. Binary indicators were derived to describe lifestyle factors and coded as follows: individuals who ever smoked were coded as 1 and those who never smoked were coded as 0; individuals who never trained their brains were coded as 1 and those who said they did were coded as 0. Similarly, individuals who did not engage in any physical training were coded as 0 and those who did were coded as 1.

We followed recommended practice to select the optimal model, including the identification of the number of classes. We fitted a series of models with an increasing number of classes and selected the best fitting model by comparing model fit indices, evaluating of entropy values and considering interpretability of each class (24). Specifically, we inspected the Bayesian Information Criterion (BIC), the sample-size adjusted BIC (SSABIC), entropy values and the Lo-Mendel-Rubin likelihood ratio test (LMR-LRT). Lower BIC and SSABIC values indicate a more parsimonious and better fitting model, whereas higher entropy values signal better class separation.

Once the best fitting model was identified, an a posteriori analysis of the distribution of twins across classes and the distribution of pairs of twins and their zygosity by class was conducted to investigate if monozygotic pairs were more likely to be assigned to the same class than dizygotic pairs.

Models were estimated in Mplus v8.0 by full maximum likelihood (FML) and robust standard errors (MLR) to non-normality and non-independence of observations (25). Missing data are assumed to be

missing at random. To avoid local maxima for the EM (expectation-maximization) algorithm, we estimated the models with up to 1000 random starting values. The MMSE is known to produce ceiling and floor effects. To investigate whether our results were sensitive to these effects, we fitted Tobit Growth Mixture models and compared results to the ones generated by the traditional GMM formulation.

Results

Our analytical sample comprised of 628 individuals, of whom 220 (35%) were men and 408 (64%) women. Women were older than men (women: 83.61 (SD=3.17) yrs. old vs men: 82.95 (SD=2.76) yrs. old, t-test, p-value=0.007) and had fewer years of education than men (women: 6.96 (SD=1.89), men: 7.51 (SD=2.90), t-test, p-value=0.01). More than 73% of the sample (n=463) remained free of dementia over the study follow-up period. See Table 1 for descriptive sample characteristics. The sample included 272 (43%) monozygotic and 356 (57%) dizygotic individuals. Sixty-three individuals (10% of total sample, 24 monozygotic and 39 dizygotic twins) were excluded due to missing data for their co-twin. Monozygotic twins were slightly more educated than dizygotic twins (7.50 (SE=0.16) years of education vs 6.89 (SE=0.10) years of education respectively, t-test, p-value=0.0009) and a larger proportion of monozygotic twins were sedentary compared to dizygotic twins (63% vs 53% respectively, chi square test, p-value=0.02). Sixty per cent (60%) of monozygotic and 68% of dizygotic individuals were women.

Inspection of BIC, SSABIC, and the Lo-Mendel-Rubin likelihood ratio test values resulted in the identification of a 4-class model as the best fitting model. The entropy for this model was 0.74, a value that suggests a good discrimination of individuals into these 4 classes.

Table 1 *Descriptive statistics of the OCTO-Twin sample*

Variables	N	Mean (SD)	Baseline characteristics	N (%)
MMSE 1	*628*	*26.3 (3.9)*	*Monozygotic*	*272 (43.0)*
MMSE 2	*524*	*24.9 (6.2)*	*Female*	*408 (65.0)*
MMSE 3	*404*	*24.4 (7.1)*	*Smoker*	*248 (39.5)*
MMSE 4	*298*	*23.7 (7.5)*	*Stimulates the body*	*266 (42.4)*
MMSE 5	*217*	*22.3 (7.8)*	*Stimulates brain*	*416 (66.3)*
Education (years)		*7.5 (2.3)*	*Diagnosed with dementia*	*165 (26.3)*

MMSE 1-5 are the MMSE scores at every follow-up. SD standard deviation

MMSE trajectory classes and characteristics

First, we examine the characteristics revealed in the 4 class model (see Table 2). In Figure 1 we show a graphical illustration of the observed and estimated MMSE trajectories in our analytical sample.

Table 2 *Results from the 4- class growth mixture model that best fitted the OCTO-Twin sample*

	High performers and stable N=198		High performers with slow decline N=194		High performers with fast decline N=181		Impaired very fast decline N=55	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
Fixed effects								
MMSE Level	28.9 (0.14)	0.00	27.62 (0.32)	0.00	26.34 (0.59)	0.00	19.30 (2.18)	0.00
Baseline age	-0.08 (0.03)	0.00	-0.16 (0.07)	0.02	-0.18 (0.12)	0.12	0.28 (0.23)	0.24
Education	0.04 (0.02)	0.04	0.09 (0.08)	0.26	0.30 (0.17)	0.09	0.73 (0.62)	0.23
Women	0.26 (0.13)	0.06	0.24 (0.37)	0.51	-0.15 (0.72)	0.83	2.71 (2.26)	0.23
Dementia	-0.50 (0.09)	0.02	0.13 (0.42)	0.75	-1.18 (0.74)	0.11	-4.29 (1.28)	0.00
Linear Slope	-0.04 (0.04)	0.30	-0.31 (0.09)	0.00	-0.96 (0.14)	0.00	-2.95 (0.86)	0.00
Baseline age	0.00 (0.00)	0.60	-0.04 (0.08)	0.82	-0.02 (0.03)	0.47	-0.02 (0.09)	0.77
Education	0.00 (0.00)	0.42	-0.01 (0.02)	0.51	-0.08 (0.05)	0.11	-0.84 (0.53)	0.10
Women	0.02 (0.04)	0.61	0.03 (0.10)	0.72	0.10 (0.18)	0.57	-0.06 (1.03)	0.95
Dementia	-0.11 (0.09)	0.23	-0.76 (0.14)	0.00	-1.40 (0.18)	0.00	-0.76 (0.52)	0.15
Random effects								
Level	0.06 (0.08)	0.42	0.06 (0.08)	0.42	0.06 (0.08)	0.42	0.06 (0.08)	0.42
Linear Slope	0.02 (0.00)	0.00	0.02 (0.00)	0.00	0.02 (0.00)	0.00	0.02 (0.00)	0.00
Error	0.66 (0.06)	0.00	5.30 (0.48)	0.00	22.24 (2.43)	0.00	27.11 (3.72)	0.00

High Performers and Stable class

The largest class was comprised of 32% of the sample (n=198). A reference individual in this class is a man aged 83 years at study entry with 7 years of education with an average MMSE score at study entry of 28.9 (SE=0.1), and who remained free of dementia over the study period. The annual rate of MMSE change was only -0.04 (SE=0.04), an estimate that did not reach conventional significance thresholds. In this class, older baseline age was associated with a lower baseline MMSE performance (ß=-0.08 (SE=0.03), while education was associated with higher baseline MMSE score (ß=0.04 (SE=0.02)). Individuals who later received a diagnosis of dementia had poorer MMSE performance at study entry than individuals who remained free of dementia (ß=-0.48, SE=0.10))

High Performers with Slow Decline class

Thirty-one per cent (31%, n=194) of the sample were assigned to a class with an average MMSE score of 27.6 (SE=0.3) at study entry. Their annual decline was -0.3(0.09) MMSE points. Age was associated with poorer baseline MMSE performance, and those who ever received a diagnosis of dementia declined at a faster rate than those who remained free from dementia.

High Performers with Fast Decline class

Twenty-nine per cent (29%, n=181) of the sample was assigned to a class with a slightly lower baseline MMSE score than the other class of high performing individuals, but they declined at a faster rate. Specifically, in this class, the reference individual had an average MMSE score at study entry of 26.3 (SE=0.6) with an annual decline of -0.9 (SE=0.1) MMSE points. Individuals who received a diagnosis of dementia declined 1.4 MMSE points faster per year than those who remained non-demented. None of the risk factors emerged as significantly associated with MMSE baseline performance, nor with rate of change.

Impaired Very Fast Decline class

Finally, 8 % (n=55) of the sample was assigned to a class characterized by low baseline scores and more substantial decline. Their average MMSE score at study entry was 19.3 (SE=2.2), followed by an annual decline of -2.9 (SE=0.8). Individuals who received a diagnosis of dementia had even poorer baseline MMSE performance, compared with those who remained free from dementia. None of the other risk factors reached significance levels.

Risk factors and class assignment probability

Next, we examine the effect of risk factors in relation to the above classification (see Table 3). Compared with the high performing and stable class and as expected, older age at study entry, was associated with higher odds of being in the class of impaired performers with very fast decline. This was also the case in the two classes of high performing individuals. Women and more educated individuals had lower odds of being in the class of *High Performers with Fast decline* individuals, than in the *High Performers and*

Stable class of individuals. Individuals who did not engage in physical activity were more likely to be in the *High Performing with Fast Decline* class, compared to the *High Performing and Stable class* of individuals, a finding that suggests a partial protective effect of education and physical activity.

Table 3 Odds ratio results from multinomial model for class assignment with reference to the High Performers and Stable class

	High performers with slow decline		High performers with fast decline		Impaired very fast decline	
	OR (SE)	p	OR (SE)	p	OR (SE)	p
Baseline age	1.12 (0.06)	0.05	1.17 (0.07)	0.01	1.22 (0.09)	0.00
Education	0.92 (0.05)	0.11	0.75 (0.08)	0.00	0.75 (0.11)	0.03
Women	0.88 (0.28)	0.67	0.51 (0.18)	0.00	1.04 (0.62)	0.93
Smoking	1.18 (0.34)	0.60	0.96(0.32)	0.92	1.08 (0.57)	0.88
Stimulates the body	1.12 (0.33)	0.71	2.28 (0.60)	0.03	5.20 (2.36)	0.07
Stimulates the brain	1.31 (0.36)	0.38	1.89 (0.54)	0.10	6.73 (4.84)	0.23

OR odds ratio; *SE* standard error

Distribution of twins across classes

In the next step, we examine the distribution of twins and partners across the four classes. In the high performing and stable class there were 47 twin pairs (i.e., 94 individuals out of 198). In the classes of *High Performers with Slow Decline* and *High Performers with Fast Decline,* there were 27 twin pairs (54 individuals out of 194) and 23 pairs (46 individuals out of 181), respectively. In the class of *Impaired individuals with Very Fast Decline*, there were 4 pairs of twins (8 individuals out of 55). These numbers indicate that 47.5 % of the individuals in the *High Performers and Stable Class* in fact had a twin partner in the same class. The corresponding proportion of having a twin in the same class *was* 23.7% among the *High Performers with Slow Decline, and* 29.8% in the *class* of *High Performers with Fast Decline*. Lastly, in the *Impaired and Fast Declining* class 14.4 % of individuals had a co-twin in the same class.

In the final step we conducted posteriori analyses, to test whether zygosity was associated with the likelihood of being assigned to a certain class (see Figure 2). Our analyses, however, failed to find evidence in support of an association ($X^2_{(3}$ p=0.46), which means that the likelihood for being in a certain class was similar for MZ and same-sex DZ twins.

Discussion

In the present study we investigated the heterogeneity change trajectories in the Mini-Mental-State Examination Screening Test (MMSE, (18)) in a sample of oldest-old monozygotic and same-sex dizogtic Swedish twins. More specifically, we evaluated whether a sub-classification of individuals into various change trajectories (classes) also could provide information about the likelihood for genetic resemblance and risk factor exposures.

We first identified 4 distinct subgroups of individuals with similar change trajectories. The majority of individuals was classified into three groups with MMSE baseline scores above impairement levels, who showed a more preserved cognition or a decline at relatively slow or faster annual rate. The fourth class was comprised of individuals who at study entry already had a low MMSE score and who thereafter declined at a faster rate. This may be a consequence of a healthy survivor effect of oldest-old individuals, as the inclusion criteria also required participation of both partners in a twin pair. The overall MMSE score for the entire sample was 26.3 (SD=3.9), which suggests that many individuals had a fairly good global cognition when they entered the study.

Previous studies have investigated the heterogeneity of aging-related cognitive decline measured by the MMSE and reported the existence of groups of individuals whose trajectories follow different patterns of change (26, 27). For example, Muniz Terrera et al. (26) studied a sample of British individuals aged 75 years old and older at study entry and identified 3 distinct patterns of MMSE change, Min (28) studied a sample of healthy Koreans aged 60 and over at baseline and identified 2 groups and Leoutsakos et al. (29) analysed a sample of American adults aged 65 and over at study entry and identified 4 different MMSE patterns of change. However, differences in study designs, features of the samples tend to make comparisons difficult. For example, whether individuals with dementia at baseline or later were included, and the different rates of non- participation at follow-ups may explain some of these inconsistencies. In addition, the analytical decisions made in each study (such as the adjustment for different variables) preclude the direct comparison of published results across publications. Despite these differences, studies provide evidence of multiple and distinct patterns of MMSE change over time.

Noteworthy, our findings about the distribution of twins across the four classes showed that the majority of twins were not assigned to the same class as their co-twin. This outcome provides evidence in support of a greater role for lifestyle and environmental exposures in late life cognitive change, than for genetic influences. This is further reinforced by the finding demonstrating an independence between zygosity and class. A large effect of genetics would otherwise have shown that monozygotic twins were more likely to be assigned to the same change trajectory class. Our findings are, therefore, in support of a nurture rather than a nature effect. Yet, given the relatively small sample and the inclusion only of the oldest old age segment in our study, further research is necessary to provide better understanding of the relative contributions of genetic and environmental influences on late life cognitive change.

Furthermore, the effect of examined risk factors on class specific level and rate of change was not clear and consistent across classes. A diagnosis of dementia also showed different effects across the four classes. In the *High Performers with Slow Decline* and *High Performers with Fast Decline* classes, but not

in the class of *Impaired* and *High Performers Stable Class*, individuals who received a diagnosis of dementia declined at a faster rate than those who remained non-demented. In the *High Performers and Stable Class*, the performance at study entry was unexpectedly almost half an MMSE point below the performance of individuals who in fact later received a diagnosis of dementia. It is possible that they were diagnosed later although demonstrating a compromised cognitive health already at baseline.

Interestingly, older age at study entry emerged as negatively associated with MMSE performance only in the *High Performers with Slow Decline* and in the *High Performers Stable Class*. In the latter, we found that education had a protective effect. This is not unexpected, as other publications quite consistently have shown that education is associated with level, but not with rate of change. Further, this result is in agreement with Muniz Terrera et al. (26), who identified 3 classes of individuals with similar MMSE trajectories and reported an association of education with baseline MMSE in the class of individuals who preserved cognitive function over time, but not with baseline MMSE or rate of change in the other 2 classes. These findings are partly supportive of the theory of passive reserve (30) suggesting that individuals with higher educational attainment will consistently perform at a higher cognitive level as they age given their greater baseline cognitive reserve, although they decline at a similar rate with their lower educated peers.

Our results about the effect of lifestyle factors on the probability of class assignment provide partial support to the hypothesis that lifestyle factors may have a protective effect on cognitive function. The findings that being physically active increases the probability of being assigned to the *High Performers and Stable Class,* compared to the class of *High Performers with fast Decline,* but not to the Impaired Decliners or *High Performers with Slow Decline* is somehow unexpected. In our study, physical activity was only measured by asking participants *"Are you presently doing or have you previously done anything special to train your body or keep your body fit?".* Hence, the opportunities to detect and evaluate the long-term effect of physical activity is limited as the question only captures the individuals' engagement on physical activities closer to study entry, and less about the intensity and life-course engagement in these activities. Unfortunately, dose (intensity, duration, frequency) and mode of the activities performed (balance, flexibility, resistance) are not captured by our global question. The literature on the mechanisms by which physical activity may have a protective effect on cognitive function in old age shows that this effect varies by dose, mode and cognitive function evaluated (31).

Our study also has some other limitations. Despite that the sample size of our study is large, considering the advanced age of study participants, models with 5 and more classes failed to identify meaningful classes as the classes identified were very small classes and models failed to converge even after fixing various model parameters. Further, GMM models were fitted under a missing at random assumption which may not be fully justified. It is also most likely that our questions about engagement in physical and cognitively stimulating activities are far from optimal to capture the role of these life-style behaviors nowadays given a crucial role also for late life cognitive functioning. However, this study was initiated already in 1991, when research about their effect on cognitive health was still in early stages.

In sum, this is the first investigation based on a classification of a twin sample into distinct groups defined by their longitudinal MMSE scores. Our analyses of similarities and differences between monozygotic and same-sex dizygotic twin pairs suggest a more minor role of genetic effects in late life cognitive change.

Declarations

Ethics approval and consent to participate

The OCTO-Twin Study received approval from the Ethics Committee at the Karolinska Institute in Stockholm and from the Swedish Data Inspection Authority. Informed written consent was obtained from all participants or their relative or caregiver where capacity to consent was questionable, for example, due to severe cognitive impairment or dementia.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are not freely available, which were used under license for the current study, and so are not publicly available. However, data analytics and study materials can be shared by contacting the corresponding author.

Competing interests

The authors declare that they have no conflict of interest.

Funding

This work was funded by NIH/NIA Program Project Grant (P01AG043362; 2013-2018).

The OCTO Twin Study was originally supported by a grant from NIA (AG 08861).

Authors' contributions

GM designed the project, performed the main analysis and wrote the paper. AR contributed to the discussion of the paper and editing. JG contributed to the data analysis, contributed to the discussion and edited the paper. FM contributed to the discussion and editing of the paper. BJ designed and collected the data and contributed to the discussion and editing of the paper.

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Figures

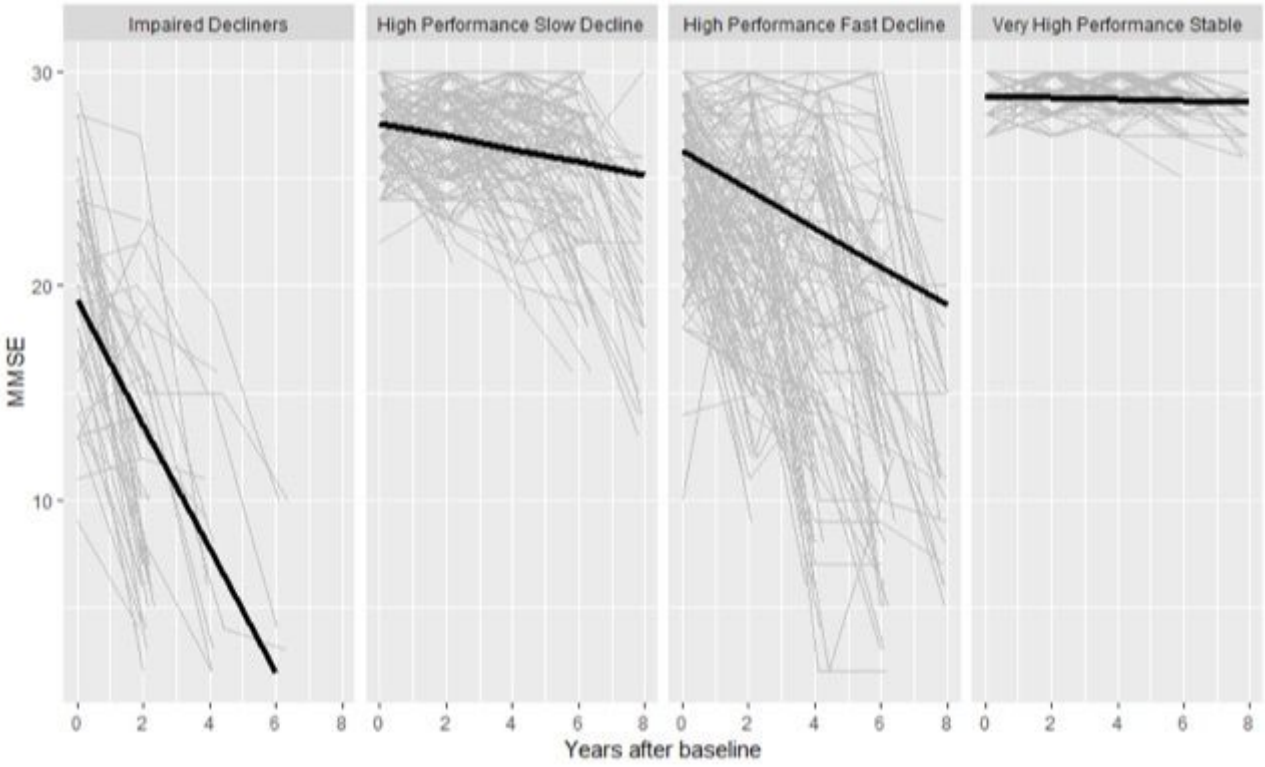

Figure 1

MMSE observed and model predicted class-specific trajectories plotted as a function of time (years past since baseline)

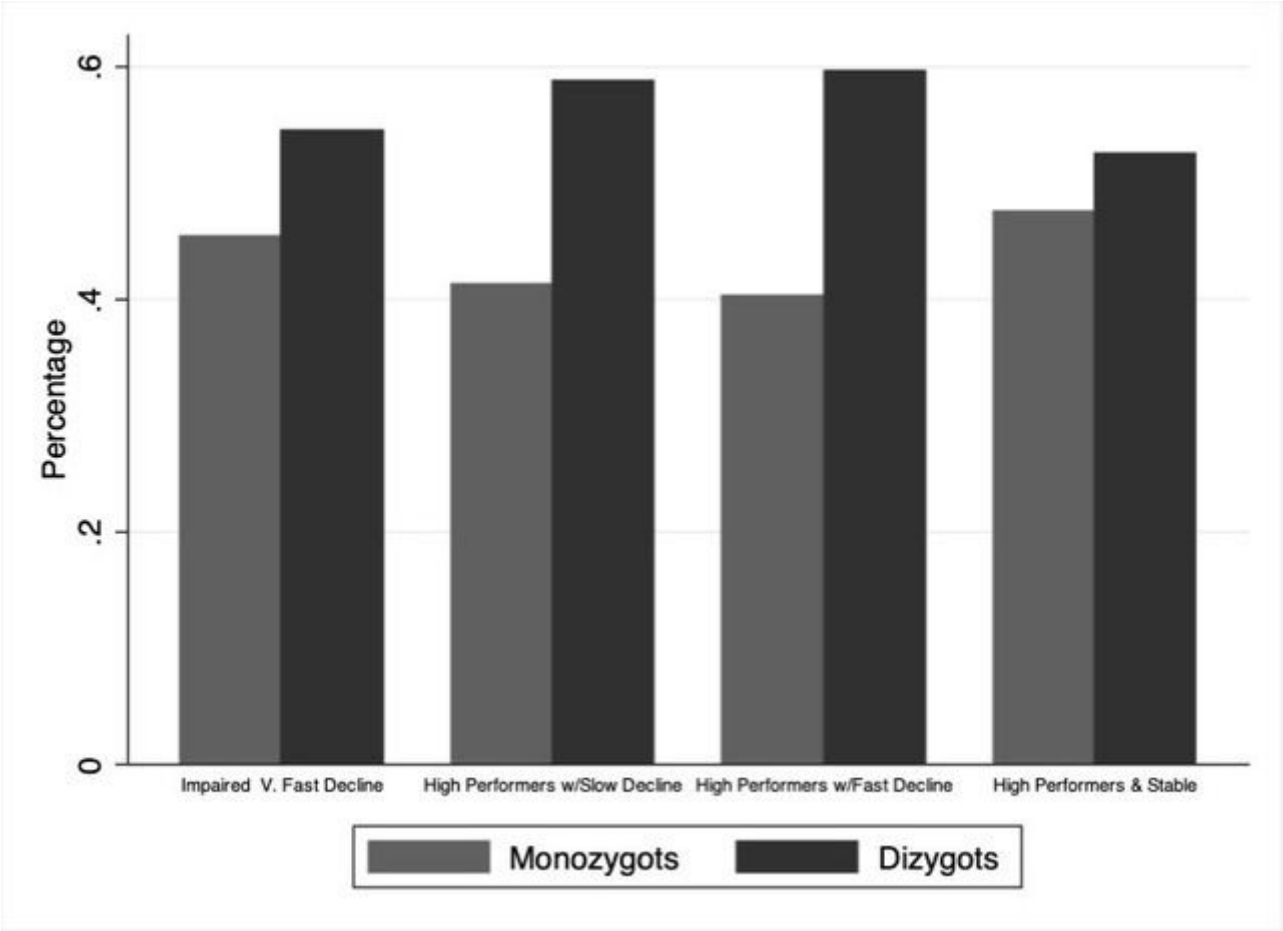

Figure 2

Frequency of Monozygotic and Dizygotic Individuals across MMSE classes