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IQ as Moderator of Terminal Decline in Perceptual and Motor Speed, Spatial, and Verbal Ability: Testing the Cognitive Reserve Hypothesis in a Population-Based Sample Followed from Age 70 until Death

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Abstract

Terminal decline (TD) refers to acceleration in within-person cognitive decline prior to death. The cognitive reserve hypothesis postulates that individuals with higher intelligence quotient (IQ) are able to better tolerate age-related increase in brain pathologies. On average they will exhibit a later onset of TD, but once they start to decline their trajectory is steeper relative to those with lower IQ. We tested these predictions using data from initially non-demented individuals (n = 179) in the H70-study repeatedly measured at ages 70, 75, 79, 81, 85, 88, 90, 92, 95, 97, 99, and 100, or until death, on cognitive tests of perceptual-and-motor-speed, spatial and verbal ability. We quantified IQ using the Raven's Coloured Progressive Matrices (RCPM) test administrated at age 70. We fitted random change point TD models to the data, within a Bayesian framework, conditioned on IQ, age of death, education, and sex. In line with predictions, we found that one additional standard deviation on the IQ scale was associated with a delay in onset of TD by 1.87 (95% HDI [0.20, 4.08]) years on speed, 1.96 (95% HDI [0.15, 3.54]) years on verbal ability, but only 0.88 (95% HDI [-0.93, 3.49]) year on spatial ability. Higher IQ was associated with steeper rate of decline within the TD phase on measures of speed and verbal ability, while results on spatial ability were non-conclusive. Our findings provide partial support for the cognitive reserve hypothesis and demonstrate that IQ can be a significant moderator of cognitive change trajectories in old age.

Keywords: Terminal decline, cognition, cognitive reserve, intelligence quotient (IQ)

The cognitive reserve hypothesis (see e.g., Stern, 2012) suggests that intellectually more able individuals can better cope with brain pathologies and therefore exhibit a later onset of cognitive decline in older ages. The hypothesis proposes a threshold model to cognitive aging, where the degree of neuropathology required for a behavioral manifestation, e.g. in the form of decline on cognitive testing, is higher for the more able individuals in comparison to the less able. The hypothesis also postulates a steeper rate of decline among the more able individuals after the onset of the decline which is assumed to reflect a relatively larger severity of the brain pathologies. Prior to the onset of the decline, the more able individuals are assumed to have a larger and a more complex network of neuronal connections in addition to more efficient cognitive strategies that can compensate the neural damages (e.g., in the form of senile plaques, neurofibrillary tangles, neuronal loss, and white-matter hyperintensities).

The terminal decline (TD) hypothesis (Kleemeier, 1962; for review see Bäckman & MacDonald, 2006) assumes a non-linear cognitive aging change trajectory with an onset of accelerated decline some years prior to death. Data from several longitudinal aging studies have been used to successfully identify and model a TD phase using various methods of change point modelling techniques (see e.g., Sliwinski et al., 2006; Wilson, Beck, Bienias, & Bennett, 2007). These studies have revealed a substantial variability in the onset of TD across different cognitive abilities (Batterham, Mackinnon, & Christensen, 2011; Dodge, Wang, Chang, & Ganguli, 2011; MacDonald, Hultsch, & Dixon, 2011; Thorvaldsson et al., 2008; Wilson, Beckett, Bienias, Evans, & Bennett, 2003) and individuals (Muniz-Terrera, van den Hout, Piccinin, Matthews, & Hofer, 2013). In addition, findings from Yu et al. (2013) show that the onset of the TD is systematically related to the apolipoprotein E (APOE) genotype. The presence of the e4 allele is associated with earlier onset of the decline. This study also demonstrated that the association between APOE and TD is partly mediated by markers of

Alzheimer's disease (AD) related neuropathology (i.e. post-mortem quantification of accumulation of amyloid and neurofibrillary tangles). Together these studies reveal that the pattern of change in the various cognitive domains prior to death is relatively similar to those observed prior to the diagnosis of dementia (e.g., Hall, Lipton, Sliwinski, & Stewart, 2000; 2001; Howieson et al., 2008; Thorvaldsson et al., 2011; Yu et al., 2012) and are thought to reflect, at least partly, the same or similar underlying mechanisms and combinations of determinants.

Batterham et al., (2011) and Muniz-Terrera et al., (2014) tested predictions of the cognitive reserve hypothesis in the context of TD using the number of years of formal school education as a proxy of cognitive reserve. Muniz-Terrera et al., found support for the hypothesis, as one additional year of school education was associated with 0.4 year delay in the onset of the TD phase and a somewhat steeper decline within the TD period on a brief measure of global cognition (the Mini Mental State Examination test). However, the findings from the Batterham et al., study provided only limited support for the hypothesis. Although longer education was indeed associated with a delayed onset of TD and a steeper rate of decline within the TD period in a measure of speed of processing, no such associations were found on measures of either global cognition or episodic memory.

The length and quality of formal school education should partly contribute to the establishment of individual differences in cognitive reserve as education increases cognitive flexibility and performance (e.g., Cliffordson & Gustafsson, 2008) and is generally associated with health behaviors that are known to be neuroprotective. However, educational attainment can also be expected to be associated with several other, more or less confounded factors (that maybe difficult to control for), such as individual differences in motivational interest, educational opportunities, and parents' socio-economic status, that may reduce its validity as a proxy of cognitive reserve. Another commonly used proxy of individual differences in

cognitive reserve (see e.g., Corral, Rodrigues, Amenedo, Sanchez, & Diaz, 2006) is intelligence quotient (IQ) test scores. Several IQ measures, such as the Raven Progressive Matrix test, have moderate correlation with measures of in vivo brain volume (see McDaniel, 2005), cortical thickness (Narr et al., 2006), and neural efficiency (see Neubauer & Fink, 2009), and a somewhat higher correlation with behavioral measures such as educational performance, occupational outcomes, and efficiency of ever-day decision making (see Strenze, 2007; Gottfredson, 1997). These are all variables that are generally assumed to be related to cognitive reserve. Furthermore, individual rank orders of IQ scores are found to be relatively constant across the lifespan (Deary et al., 2000), which further supports the validity of IQ scores as a proxy of cognitive reserve in old age.

In this study, we quantified individual differences in cognitive reserve using the Raven Coloured Progressive Matrix test (i.e., a sub-test of the original standard version). More specifically, we evaluated the role of IQ as a moderator of TD on three cognitive outcomes, i.e., perceptual and motor speed, spatial ability and verbal ability. Data was drawn from the H70 study (see Rinder, Roupe, Steen, & Svanborg, 1975), in which an initially non-demented age-homogenous (i.e., all born within one year interval) representative population-based sample was examined first at age 70, and then repeatedly followed at 12 occasions over 30 years or until death. We fitted random change point TD models to the data, within a Bayesian framework using non-informative prior distributions, conditioning the onset of the TD (i.e., the change point), change prior to and within the TD phase, on the measures of IQ, age of death, education, and sex.

Method

Participants

We drew the data from the Gerontological and Geriatric Population Studies in Gothenburg, Sweden (H70; see Rinder et al., 1975; Svanborg, 1977). In 1971, the total population, born

between July 1st, 1901 and June 30th, 1902 (i.e., at age 70), living in the city of Gothenburg, was identified from the Swedish Revenue Office Register. Approximately one-third (n = 1148) of this population (i.e., individuals born on days ending with the numbers 2, 5, and 8) was systematically selected and offered participation in the study. The baseline participation rate of the total sample was 85%. Of this sample, 40% (n=460) were randomly selected for participation in the psychometric examination. Then, 50% (n=230) of this sub-sample was randomly selected for further cognitive testing at ages 70, 75, 79, 81, 85, 88, 90, 92, 95, 97, 99, and 100, including the Raven test at age 70. Baseline participation rate for this sub-sub-sample was 79% (n = 182). Two of these were diagnosed with dementia at baseline and one contributed only to the Raven test data. These three participants were omitted from the analyzed sample (n = 179). Non-mortality dropout rate for this sample varied across occasions from 6.7% in 1976 (age 75) to 0% on all occasions after 1993. 37 (20.7%) participants contributed data on only 1 occasion, 50 (27.9%) on 2 occasions, 20 (11.2%) on 3 occasions, 33 (18.4%) on 4 occasions, 15 (8.4%) on 5 occasions, 6 (3.4%) on 6 occasions, 11 (6.1%) on 7 occasions, 2 (1.1%) on 8 occasions, 3 (1.7%) on 9 occasions, 1 (0.6%) on 10 occasions, and 1 (0.6%) on 12 occasions. Mean number of contributed occasions was 3.25 (SD=2.12) and mean years of follow-up 11.65 (SD=6.42). Variable indicating years from last occasion to death was highly skewed with a median of 2.4 years and mean of 3.8 years (SD=4.3). 18.6% of the participants were deceased within 1 year from their last measurement occasion, 41.2% within 2 years, 57.1% within 3 years, 72.2% within 4 years, 79.1% within 5 years, 92.1% within 6 years. The H70 data was collected in compliance with the ethic review committee at the University of Gothenburg.

IQ measure

We used the Raven Coloured Progressive Matrix (RCPM) test as a marker of IQ. This test is a shorter and simplified version of the Raven Standard Progressive Matrix test (Raven, 1960),

adapted especially for the testing of older adults (for evaluation of psychometric properties of this version see e.g., Carlson & Jensen, 1981; Cotton et al., 2005). The RCPM is a non-verbal test, where participants are asked to find the logical solution concerning the relationship among figures. For each problem, the participants are presented with one target figure where one of the pieces is missing. The task is to select the correct figure among six or more alternatives. The test consists of 36 problems, divided into three sets (A, Ab, B), with 12 problems each. Within, and across, the sets, the problems become progressively more difficult. An essential part of the test is to gradually develop a method of reasoning that helps the participant to solve the more difficult problems. The Raven tests are generally considered to have good psychometrical properties with relatively high loading on a general intelligence factor (see e.g., Carpenter, Just, & Schell, 1990). For purpose of our analyses, we calculated a summary score based on the three sets (see Table 1). The summary score was used as an IQ index and assumed a proxy of cognitive reserve. The distributions of the RCPM test scores in the H70 (Anderson, Berg, Lawenius, & Svanborg, 1978) are comparable to norms as reported from other comparable population-based elderly samples (see e.g., Smits, Smit, Heuvel, & Jonker, 1997).

Covariates

Date of death was obtained from the Swedish Population Register (Statistics Sweden). The average age of death was 83.44 (SD = 7.50). We generated a composite score of education from two questions. The first asked about completed degree of formal school education: 0 = less then compulsory education (which was 6 years for this birth cohort); 1 = compulsory education (*folkskola*); 2 = compulsory education + uncompleted high school (*gymnasium*) or comparable (i.e., *folkhögskola, realskola, flickskola*); 3 = high school diploma (*studentexamen*); 4 = uncompleted university studies; 5 = university diploma. Additionally, we added one extra point to this scale if the participants reported they had acquired additional

education as part of their occupation and working career development. The mean value of this scale was 1.37 (SD = 0.81), reflecting that the vast majority of this cohort only completed compulsory education. Of the sample, 58% was female.

Specific cognitive measurements

The cognitive tests used in the H70 study are based on Thurstone's (1938) theory of primary mental abilities and included in the Dureman and Sälde (1959) test battery, widely used in Sweden at the time when the H70 study was initiated. For the purpose of the presented analyses, we excluded four tests form the original test battery due to poor psychometrical properties (i.e., Digit Span Forward and Backward) and lack of number of follow-ups (i.e., Figure Logic and Thurstone's Picture Memory).

Figure Identification is a measure of perceptual- and motor-speed. Participants are asked to match, as quickly as possible, a target figure with one identical figure placed in line among four others. The total raw score is calculated as Total correct items – (Total wrong items/4), in order to penalize wrong answers and guessing. The maximum score is 60 and the time limit is 4 minutes.

Block Design measures spatial ability. Participants are given colored blocks and asked to construct replicas of prototype model designs presented to the participants in two colors. Seven prototypes are presented with an increasing difficulty. The performance is scored based on how fast the participants correctly replicated the prototypes. The maximum score is 42 and the total time limit is 20 minutes.

Synonyms measure verbal ability, or the ability of comprehension of the meaning of words. Participants are asked to match a target word with one synonym among five choices. The maximum score is 30 and the time limit is 7 minutes. The words are presented in a magnified form to avoid visual problems.

The Synonym test was administered at all occasions, i.e., at ages 70, 75, 79, 81, 85, 88, 90, 92, 95, 97, 99, and 100. The Block Design test was omitted at age 81 and the Figure Identification test was omitted at age 81 and 100. Bivariate correlations between the RCPM test and the Figure Identification, Block Design, and Synonyms tests at age 70 were 0.46, 0.62, and 0.43, respectively. Further information about these tests and their psychometric properties can be found in Dureman, Kebbon, & Österberg (1971) and their usage in the H70 study in Berg (1980).

Statistical analyses

We fitted random change point growth curve models to the data using a Bayesian framework (see e.g., Gelman et al., 2014). These are essentially two slope spline mixed effects models (see e.g., Hall et al., 2000). We specified the time component in all models as -1 times years to death (i.e., TTD) and regressed level 1 coefficients on all level 2 coefficients included in the respective model. We can write the model as:

Level 1:

$$Cognition_{ti} = \beta_{0i} + \beta_{1i}(TTD_{ti} + \beta_{3i})[1 - I(TTD_{ti} + \beta_{3i})] + \beta_{2i}(TTD_{ti} + \beta_{3i})[I(TTD_{ti} + \beta_{3i})] + \varepsilon_{ti}$$

Level 2:

$$\beta_{0i} = \gamma_{00} + \gamma_{01}IQ_i + \gamma_{02}AGED_i + \gamma_{03}EDU_i + \gamma_{04}SEX_i + U_{0i}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}IQ_i + \gamma_{12}AGED_i + \gamma_{13}EDU_i + \gamma_{14}SEX_i + U_{1i}$$

$$\beta_{2i} = \gamma_{20} + \gamma_{21}IQ_i + \gamma_{22}AGED_i + \gamma_{23}EDU_i + \gamma_{24}SEX_i + U_{2i}$$

$$\beta_{3i} = \gamma_{30} + \gamma_{31}IQ_i + \gamma_{32}AGED_i + \gamma_{33}EDU_i + \gamma_{34}SEX_i + U_{3i}$$

where the cognition (e.g., perceptual and motor speed, spatial ability, or verbal ability) outcome data points at time $t = 1,\ldots, n_i$ are nested within individuals $i = 1,\ldots, N$. We can

interpret the β_{0i}, β_{1i}, and β_{2i} as the estimated level of cognitive performance at the time of the change point (i.e., the onset of terminal decline), the linear slope prior to the change point, and the linear slope after the change point, respectively, for individual *i*. The β_{3i} is the change point for individual *i* and *I* is an indicator function, such that, $I(TTD_{ti} + \beta_{3i}) = 1$, if $TTD_{ti} + \beta_{3i} \geq 0$, and otherwise 0. The ε_{ti} is level 1 residual, assumed to take normal distribution with mean 0 and estimated variance. The U_{0i}, $U_{1i,}$ $U_{2i,}$ and $U_{3i,}$ are the level 2 variability components for the intercept, slope prior to the change point, slope after the change point, and the change point, respectively. These are assumed to take normal distribution with mean 0 and an estimated and unstructured variance/covariance matrix. The IQ_i, $AGED_i$, EDU_i, and SEX_i are the RCPM test score, age of death, educational level, and sex for the individual *i*. These level 2 covariates were mean centered. We note that this parameterization imposes continuity in the individual change trajectories and centers the intercept at time of the individual change point. For review of alternative parameterizations of random change point models see Muniz-Terrera & Hall (2016). We specified the priors for the level 2 gamma parameters (γs) as normal distributions with mean 0 and standard deviation 100. For the level 1 residual we used uniform priors with a minimum value of 0 and a maximum value of 100. We used scaled inverse Wishart priors with 5 degrees of freedom to model the level 2 residual variance/covariance matrix. Parameters were derived through numerical approximation using Markov Chain Monte Carlo Gibbs sampling in JAGS (Plummer, 2003). For each model, we used 2 chains, each with 900000 iterations, a burn-in of 450000, and a thinning factor of 10, resulting in 90000 iterations (i.e., 45000 from each chain) to approximate the posterior distribution. We note that such a large number of iterations were not needed for the models fitted to the perceptual and motor speed and the verbal ability test data. However, we encountered estimation difficulties in the model fitted to the spatial ability data, requiring at least this many iterations. We used the medians of the marginal posterior density distribution

as point estimates and the 95% highest density interval (HDI), defined as the 0.025 and 0.975 quantiles, as precision estimates. Occasional missing data on the dependent variable were assumed to be missing at random, as conventionally defined, given the model. There were no missing data on the covariates.

In order to evaluate the convergence of each chain on the target distribution we generated trace plots, plotted the auto-correlation trends, and plotted the marginal posterior probability density functions separately for each of the two chains used in the numerical approximation (as to compare the overlap) for all evaluated parameters. These diagnostics indicated good to adequate convergence of the chains to the target distributions for almost all parameters, with the exception of several parameters in the spatial ability test model in which these diagnostics indicated a relatively poor mixing across the chains. Due to this, we contemplated the possibility of omitting the spatial ability test from the report. However, given that we had conducted these analyses and our judgment was that the results bear some information of concern for testing of the cognitive reserve hypothesis, we decided to keep the test while explicitly reporting the estimation difficulties. This implies that the results should be interpreted with substantial caution. Additionally, to evaluate whether the selected priors were influencing our estimates in unintended ways, we conducted several sensitivity analyses by varying the specification of the prior distributions.

Results

Estimates from the random change point TD models are shown in Table 2. We can interpret the intercept (i.e., level 2) in these models as the estimated average level of performance at the time of the onset of the TD for the respective cognitive ability (i.e., conditioning on the level 2 covariates that are all mean centered). The IQ, age of death, education, and sex coefficients refer to the conditioned deviation from that level of performance. For the perceptual and motor speed test, one additional value on the IQ scale was associated with a 0.74, 95% HDI

[0.40, 1.07], point higher value at the time of the onset of the TD (i.e., 15.51, 95% HDI [11.72, 21.01] years prior to death), after accounting for individual differences associated with age of death, education, and sex. The corresponding estimates were 0.49, 95% HDI [0.25, 0.75], for spatial ability and 0.58, 95% HDI [0.37, 0.77], for verbal ability, indicating, as expected, that those with higher IQ values tend, on average, to perform better on all the cognitive measures. Higher values on the education scale was associated with 2.09, 95% HDI [0.12, 4.31], points better performance on measures of perceptual and motor speed, and 2.45, 95% HDI [1.21, 3.83], points better performance on spatial ability. This finding, however, was not replicated for the verbal ability test, 0.69, 95% HDI [-0.46, 1.85]. Age of death and sex were not significantly associated with level of performance at the time of the onset of the TD.

We can interpret the Slope 1 coefficient as the estimated average linear rate of change before the onset of the TD phase. This estimate was close to zero for perceptual and motor speed and verbal ability, but negative, indicating average decline, -0.21, 95% HDI [-0.39, -0.05], for spatial ability. Higher IQ values where associated with a higher estimate on this slope for perceptual and motor speed, 0.10, 95% HDI [0.01, 0.36], indicating gains in performance for those above average on the IQ scale. This estimate was small and negative for spatial ability, -0.03, 95% HDI [-0.04, -0.01], indicating a somewhat steeper decline prior to the TD among those with higher IQ values. This estimate was however non-significant for verbal ability. Age of death additionally moderated the pre TD slope, 0.12, 95% HDI [0.04, 0.33], where those with age of death above average (83.44) had estimates of gains prior to the TD phase on the perceptual and motor speed test but not on spatial and verbal ability. Neither education nor sex had any significant moderating effect on this coefficient.

The Slope 2 coefficients refer to the estimated average linear rate of change within the TD phase. This estimate was negative and significant for all the outcome variables, indicating

a substantially steeper average decline within the TD period as compared with the rate of change prior to the onset of TD (i.e., Slope 1). These estimates were: -0.69, 95% HDI [-0.90, -0.52], for perceptual and motor speed; -1.52, 95% HDI [-3.06, -0.79], for spatial ability; and -1.63, 95% HDI [-2.69, -0.82], for verbal ability. Higher IQ values were associated with steeper decline within the terminal decline period on measures of perceptual and motor speed, -0.03, 95% HDI [-0.06, -0.01], and verbal ability, -0.10, 95% HDI [-0.18, -0.01], but not spatial ability, -0.05, 95% HDI [-0.15, 0.11]. These estimates have relevance for the predictions derived from the cognitive reserve hypothesis. To further examine this we plotted the marginal probability density posterior distributions of these parameters in Figure 1a-c. As shown in these plots, the evidence is strongly in favor of the reserve hypothesis for the perceptual and motor speed and verbal ability measure (i.e., most of the probability density falls below the zero value), but less so for spatial ability. Neither age of death nor sex showed any significant associations with rate of change within the TD phase, but, higher values on the education scale was associated with steeper decline on perceptual and motor speed, -0.19, 95% HDI [-0.36, -0.04], and verbal ability, -0.42, 95% HDI [-0.79, -0.03], but not spatial ability, -0.37, 95% HDI [-0.88, 0.05].

The change point coefficients refer to average onset of TD, in years prior to death, on the respective cognitive outcome variable. These estimates were: 15.51 years, 95% HDI [11.72, 21.01], for perceptual and motor speed; 3.69 years, 95% HDI [2.28, 6.86], for spatial ability; and 3.17 years, 95% HDI [0.15, 4.21], for verbal ability. Higher IQ values were significantly associated with a later onset of TD on measures of perceptual and motor speed, -0.38, 95% HDI [-0.83, -0.04], and verbal ability, -0.40, 95% HDI [-0.72, -0.03], but not spatial ability, -0.18, 95% HDI [-0.71, 0.19]. These parameters also have relevance to the predication derived from the cognitive reserve hypothesis. We have therefore plotted the marginal probability density posterior distributions of these parameters in Figure 2a-c. As

shown in these figures, the evidence is in favor of the reserve hypothesis on measures of perceptual and motor speed and verbal ability, but less so for spatial ability. Age of death was associated with earlier onset of TD on all cognitive outcomes (0.76, 95% HDI [0.42, 1.07], 0.18, 95% HDI [0.00, 0.39], 0.24, 95% HDI [0.02, 0.50], for perceptual motor speed, spatial ability, and verbal ability, respectively). This indicates a longer TD phase for those who died at higher ages. Neither education nor sex significantly moderated the change point.

In Figure 3a-c we plot the individual raw score change trajectories with overlaid fixed effects estimates from the final models and vertical lines indicating the placement of the estimated change points. For purpose of demonstration, we stratified the sample such that those with IQ scores below the 0.25, between the 0.25 - 0.75, and above the 0.75 quantiles, take color red, green, and blue, respectively. The plotted fixed effects (bold lines) are based on 1 SD below the mean, the mean, and 1 SD above the mean on the IQ scale, taking color red, green, and blue, respectively, and centering other covariates at their mean levels.

Discussion

We tested two predictions derived from the cognitive reserve hypothesis concerning cognitive aging in the context of TD. The reserve hypothesis predicts that individual difference in IQ is associated with onset of TD and rate of decline within the TD period. Those with higher IQ are assumed to show a later onset of TD and a steeper decline thereafter in comparison with those with lower IQ. We quantified individual differences in IQ using the RCPM test and fitted random change point TD models to the cognitive data drawn from a representative population-based age-homogenous sample followed from age 70 until death. Our findings largely corroborate the cognitive reserve hypothesis—higher IQ was associated with later onset of the TD and a steeper decline thereafter on measures of perceptual and motor speed and verbal ability. However, the findings from the spatial ability measure were less certain due to estimation difficulties.

As demonstrated in Figure 3a-c, increment of one standard deviation on the IQ test was associated with a delay in the onset of the TD phase by 1.87 (i.e., 4.91*0.38) (95% HDI [0.20, 4.08]) years on the perceptual and motor speed, 0.88 (95% HDI [-0.93, 3.49]) year on spatial ability, and 1.96 (95% HDI [0.15, 3.54]) years on verbal ability. The reserve hypothesis accounts for these patterns of findings by postulating that those with higher IQ, on average, tend to have larger and more robust networks of neural connections and better cognitive strategies, that allow them to retain intact cognitive performance despite the accumulation of brain pathologies. Another, but perhaps less possible, explanation could be that the accumulation of brain pathology in old ages occurs closer to death among the intellectually more able, but when it occurs it accumulates at a faster rate. Unfortunately, we have no index of brain pathology in our sample that allows us to directly test and distinguish between these two alternative explanations.

Another interesting aspect of our findings is that age of death was significantly associated with TD onset on all cognitive outcomes, indicating that those who live longer in fact also tend to experience a more extended TD phase. Given the well-known secular changes in life-expectancy (e.g., Oeppen & Vaupel, 2002), where the later born cohorts tend on average to live longer, we could expect based on our findings, that a larger proportion of the aging population will be in TD in future birth cohorts. The evidence supporting this is however sparse and the average cognitive TD trajectories in old age may be expected to differ among birth cohorts (c.f. Hülür, Infurna, Ram, & Gerstrof, 2013).

Contrary to predictions from the cognitive reserve hypothesis, education was not associated with the onset of TD in our sample. This could be explained by the restricted variance on this variable in the H70 data, as the vast majority only completed the compulsory education level of six years. The effect of education is also likely to be partly mediated by the inclusion of IQ in the models. To further evaluate this possibility we fitted additional models

to the data after omitting the IQ variable. These analyses revealed only minor moderating effects of education on the TD onset and the pre and post TD slopes. In line with findings from other population-based studies (Cadar et al., 2016; Piccinin, et al., 2013) the moderating effect of education on cognitive change in old age is small.

Other studies have shown that neuropathological indices of Alzheimer disease, cerebrovascular disease, and Lewy body disease (i.e., the most common types of dementia in old age) together account for a relatively small proportion (i.e., about 1/3) of the between-person variability in TD (Boyle, et al., 2013). We should, however, not expect that these pathologies can account for the total between-person TD variability in any single model, due to several other confounding factors such as short-term variability in the cognitive outcomes, unreliability in the cognitive and pathological measurements, lack of precision in identification of the change points, and model misspecification, which may contribute to the pileup of such residuals. The proportions reported by Boyle et al., may though seem low, and indicate the potential role of unknown neuropathological markers as discussed by Wilson, Leurgans, Boyle, Schneider, & Bennett (2010). However, we should also expect that behavioral markers of cognitive reserve, such as IQ, can significantly contribute to the explanation of individual differences in TD, as was demonstrated in this study.

Some of the main strengths of this study are that we used a sample that was systematically selected from a general population, repeatedly measured on multiple occasions on three abilities, covering different aspects of human cognition, with complete and reliable information about age of death. We used statistical models that fit the theoretical framework of cognitive TD and allow straightforward testing of the predictions derived from the cognitive reserve hypothesis in the form of marginal probability density posterior distributions of the parameters of interest. Also, we used a well-established test of IQ as a marker of cognitive reserve while controlling for education, age of death, and sex.

The limitations include a small sample size (n=179) and long time between some of the testing occasions (varying from 1-5 years). These are both factors that may limit inferences and generalization from the H70 data. The long time in-between testing occasions (in addition to retest effects) may, for example, contribute to our findings of an unusually long TD phase in the perceptual and motor speed test. We note however that this unusually long TD phase is a character of the H70 data and not an artifact due to the model specification or estimation procedure used in the analyses. Similar length in the TD phase are found using other analytical procedures, such as a fixed change point TD model (Thorvaldsson et al., 2008) or a quadratic polynomial function TD model (Thorvaldsson, Hofer, & Johansson, 2006), even when fitted to the sub-sample data used in the present study. Additionally, we encountered computational difficulties in the numerical approximation of the posterior distribution for the model fitted to the spatial ability test data. For example, indicated by skewed marginal probability density posterior distributions of some of the variability components in this model and a relatively poor fit to the data (as shown in Figure 3b). Estimates from the model fitted to spatial ability should therefore be interpreted with substantial caution. Also, our IQ measures should ideally have been conducted at an earlier age. Although none of our participants were clinically diagnosed with dementia at baseline, it is likely that some were affected by neuropathologies that could have influenced their IQ scores, as well as the other cognitive measures. Despite these shortcomings, we are confident that our findings provide a contribution to the evaluation of the cognitive reserve hypothesis and the determinants of cognitive TD in old age.

The observed individual change trajectories and estimates revealed in this study must be interpreted in the context that older adults can learn and thereby gain in performance due to previous exposure to the testing situations (i.e., retest or practice effects). Given the design of the H70 study, we are not in a position to separate variability related to learning gains from

within-person aging changes. To sufficiently do so, would require measurements and proper quantification of the learning gains in addition to repeated follow-ups over a sufficiently long period of time in order to capture the aging trends. Models that include a variable counting the individual's number of measurements, or dummy variables indexing number of occasion, as control for retest effects, rely on strict assumptions (e.g., no cohort effects or selective mortality attrition) that we find unrealistic in most cognitive aging studies (for further discussion of this issue see e.g., Hofer & Sliwinski, 2006; Thorvaldsson, 2016). These models further require sufficient between-person age-heterogeneity in the sample to allow a reasonable estimate of the conditioned time trends and are therefore non-applicable for the presented age-homogenous data.

Conclusions

Our analyses reveal that higher IQ contributes to a delay in the onset of cognitive TD in old age. Higher IQ also seems to be related to a steeper decline within the TD phase. The findings provide partial support for the cognitive reserve hypothesis suggesting that a higher reserve can counteract and postpone the impact of age-related brain pathologies on behavioral outcomes. In order to raise each individuals potential of a lifelong cognitive trajectory in the absence of terminal decline, we suggest interventions known to improve intellectual capacities and cognitive reserve, such as cognitively stimulating activities, be integrated as part of a healthy life-style.

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Table 1. *Baseline (age 70) mean and standard deviation on the IQ test and the other cognitive measures (n=179)*

Variable	Mean (*SD*)
IQ (Raven Coloured Progressive Matrix)	
A	9.19 (1.76)
Ab	7.44 (2.38)
B	5.31 (1.64)
Total	21.96 (4.91)
Verbal ability (Synonyms)	16.78 (6.58)
Spatial ability (Block Design)	12.96 (7.06)
Perceptual and motor speed (Figure Identification)	16.10 (8.72)

Table 2. *Estimates from random change point terminal decline models with IQ, age of death, education and sex as covariates*

	Perceptual and motor speed		Spatial ability		Verbal ability	
Parameters	Posterior median	95% HDI[e]	Posterior median	95% HDI	Posterior median	95% HDI
Fixed effects						
Intercept[a]	19.08	[17.03, 22.68]	11.15	[9.73, 13.17]	17.09	[16.16, 18.03]
IQ	**0.74**	**[0.40, 1.07]**	**0.49**	**[0.25, 0.75]**	**0.58**	**[0.37, 0.77]**
Age of death	0.08	[-0.23, 0.32]	-0.06	[-0.19, 0.08]	0.03	[-0.11, 0.16]
Education	2.09	[0.12, 4.31]	2.45	[1.21, 3.83]	0.69	[-0.46, 1.85]
Sex	1.54	[-1.6, 4.57]	-0.23	[-2.30, 1.66]	0.78	[-1.03, 2.62]
Slope 1[b]	0.02	[-0.37, 0.56]	-0.21	[-0.39, -0.05]	0.00	[-0.03, 0.05]
IQ x Slope 1	**0.10**	**[0.01, 0.36]**	**-0.03**	**[-0.04, -0.01]**	**-0.00**	**[-0.01, 0.01]**
Age of death x Slope 1	0.12	[0.04, 0.33]	-0.00	[-0.01, 0.02]	0.00	[-0.01, 0.01]
Education x Slope 1	-0.01	[-0.80, 0.36]	0.04	[-0.05, 0.14]	-0.00	[-0.05, 0.03]
Sex x Slope 1	-0.02	[-0.56, 0.45]	-0.02	[-0.20, 0.10]	-0.00	[-0.04, 0.03]
Slope 2[c]	-0.69	[-0.90, -0.52]	-1.52	[-3.06., -0.79]	-1.63	[-2.69, -0.82]
IQ x Slope 2	**-0.03**	**[-0.06, -0.01]**	**-0.05**	**[-0.15, 0.11]**	**-0.10**	**[-0.18, -0.02]**

Age of death x Slope 2	0.02	[-0.01, 0.04]	0.02	[-0.06, 0.14]	0.01	[-0.06, 0.09]
Education x Slope 2	-0.19	[-0.36, -0.04]	-0.37	[-0.88, 0.05]	-0.42	[-0.79, -0.03]
Sex x Slope 2	-0.17	[-0.42, 0.08]	-0.38	[-1.46, 0.64]	-0.64	[-1.46, 0.13]
Change point[d]	15.51	[11.72, 21.01]	3.69	[2.27, 6.86]	3.17	[1.79, 4.91]
IQ x Change point	**-0.38**	**[-0.83, -0.04]**	**-0.18**	**[-0.71, 0.19]**	**-0.40**	**[-0.72, -0.03]**
Age of death x Change point	0.76	[0.42, 1.07]	0.18	[0.00, 0.39]	0.24	[0.02, 0.50]
Education x Change point	0.39	[-1.06, 2.03]	1.17	[-0.01, 2.34]	0.32	[-1.22, 1.59]
Sex x Change point	-0.81	[-4.87, 2.36]	-0.85	[-3.19, 1.01]	-0.36	[-2.91, 1.96]
Random effects (*SD*)						
Intercept	6.44	[4.87, 8.42]	4.10	[3.41, 5.03]	5.18	[4.55, 5.91]
Slope 1	0.09	[0.02,0.33]	0.05	[0.01, 0.24]	0.01	[0.00, 0.06]
Slope 2	0.41	[0.19, 0.61]	0.40	[0.10, 1.44]	0.70	[0.23, 1,15]
Change point	2.86	[1.36, 5.20]	0.93	[0.21, 4.74]	3.82	[2.53, 5.53]
Residual	3.90	[3.42, 4.45]	3.14	[2.83, 3.52]	2.48	[2.27, 2.71]

Notes. [a]Estimates of level of performance at time of the onset of terminal decline. All covariates were mean centered. [b]Linear rate of change prior to onset of terminal decline. [c]Linear rate of change within the terminal decline phase. [d]Onset of terminal decline. [e]Highest density interval.

Figure Caption

Figure 1a-c. The marginal probability density posterior distributions of the IQ interactions with linear rate of cognitive change within the terminal decline period.

Figure 2a-c. The marginal probability density posterior distributions of the IQ interactions with onset of terminal decline in the cognitive functions.

Figure 3a-c. Raw score change trajectories as a function of time to death and estimated fixed effects for individuals with 1 SD below the mean (red), mean (green), and 1 SD above the mean (blue) on the IQ measure.

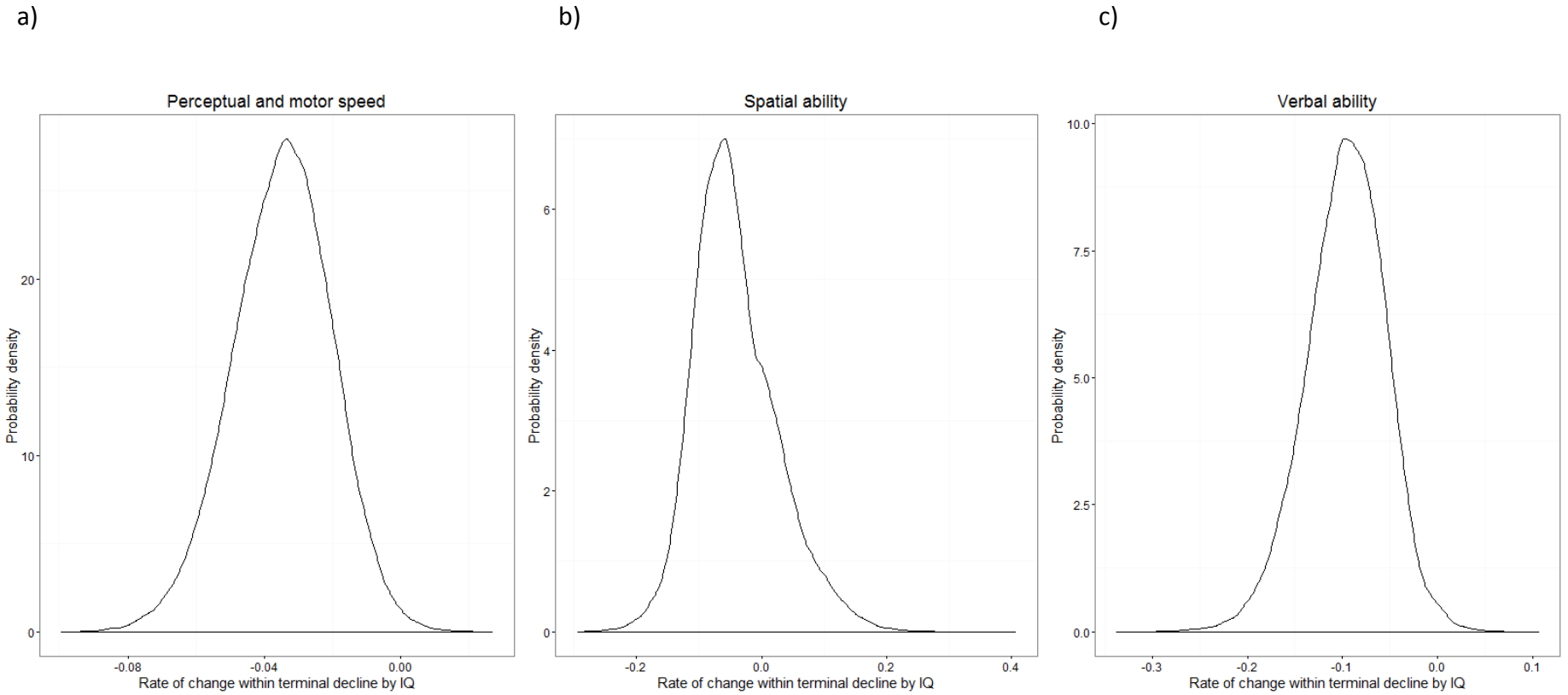
a)
b)
c)
Perceptual and motor speed
Spatial ability
Verbal ability
Probability density
Rate of change within terminal decline by IQ
0
10
20
2
4
6
0.0
2.5
5.0
7.5
10.0
-0.08
-0.04
0.00
-0.2
0.0
0.2
0.4
-0.3
-0.2
-0.1
0.0
0.1

Figure 1a-c.

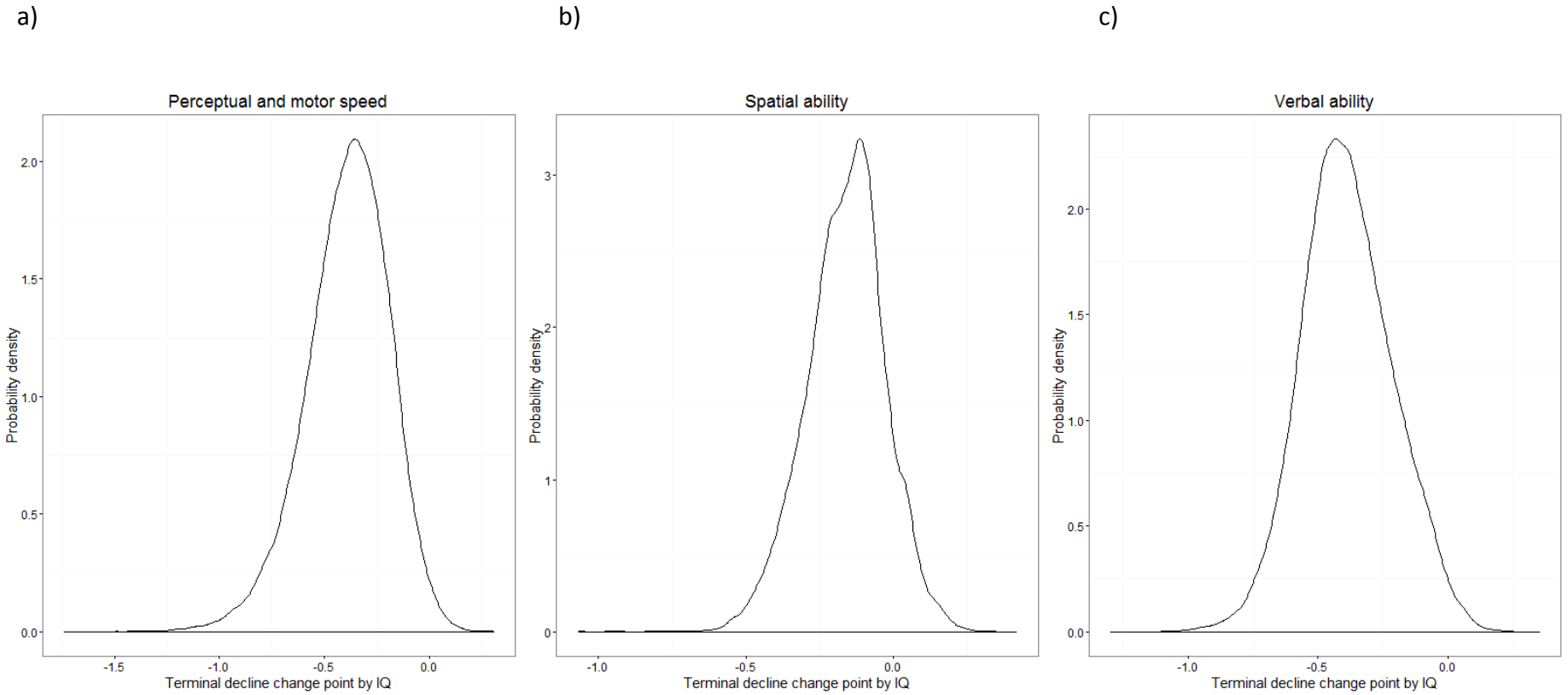
a)
b)
c)
Perceptual and motor speed
Spatial ability
Verbal ability
Probability density
Terminal decline change point by IQ
2.0
1.5
1.0
0.5
0.0
3
2
1
0
-1.5
-1.0
-0.5
0.0

Figure 2a-c.

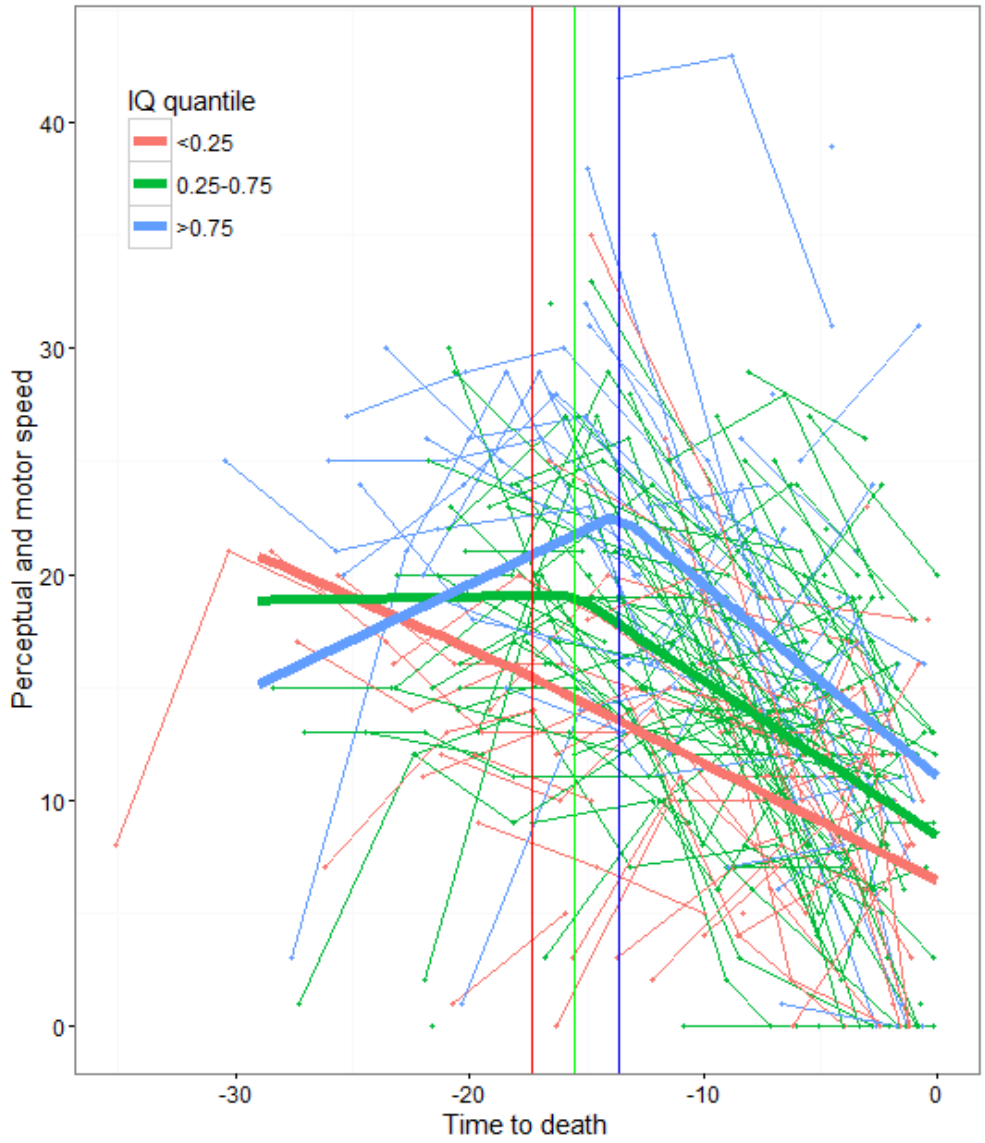
IQ quantile
<0.25
0.25-0.75
>0.75
Perceptual and motor speed
40
30
20
10
0
-30
-20
-10
0
Time to death

Figure 3a

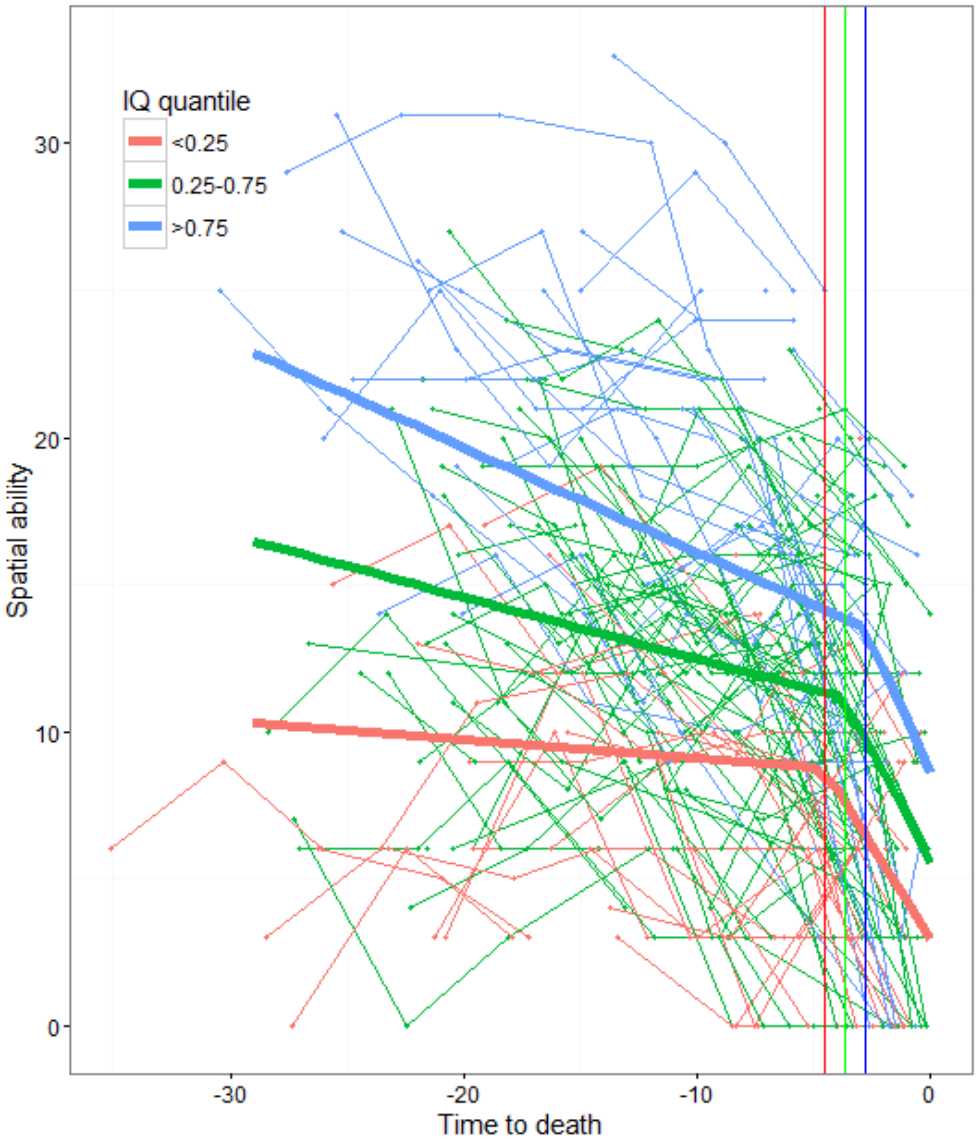
IQ quantile
<0.25
0.25-0.75
>0.75
Spatial ability
30
20
10
0
-30
-20
-10
0
Time to death

Figure 3b

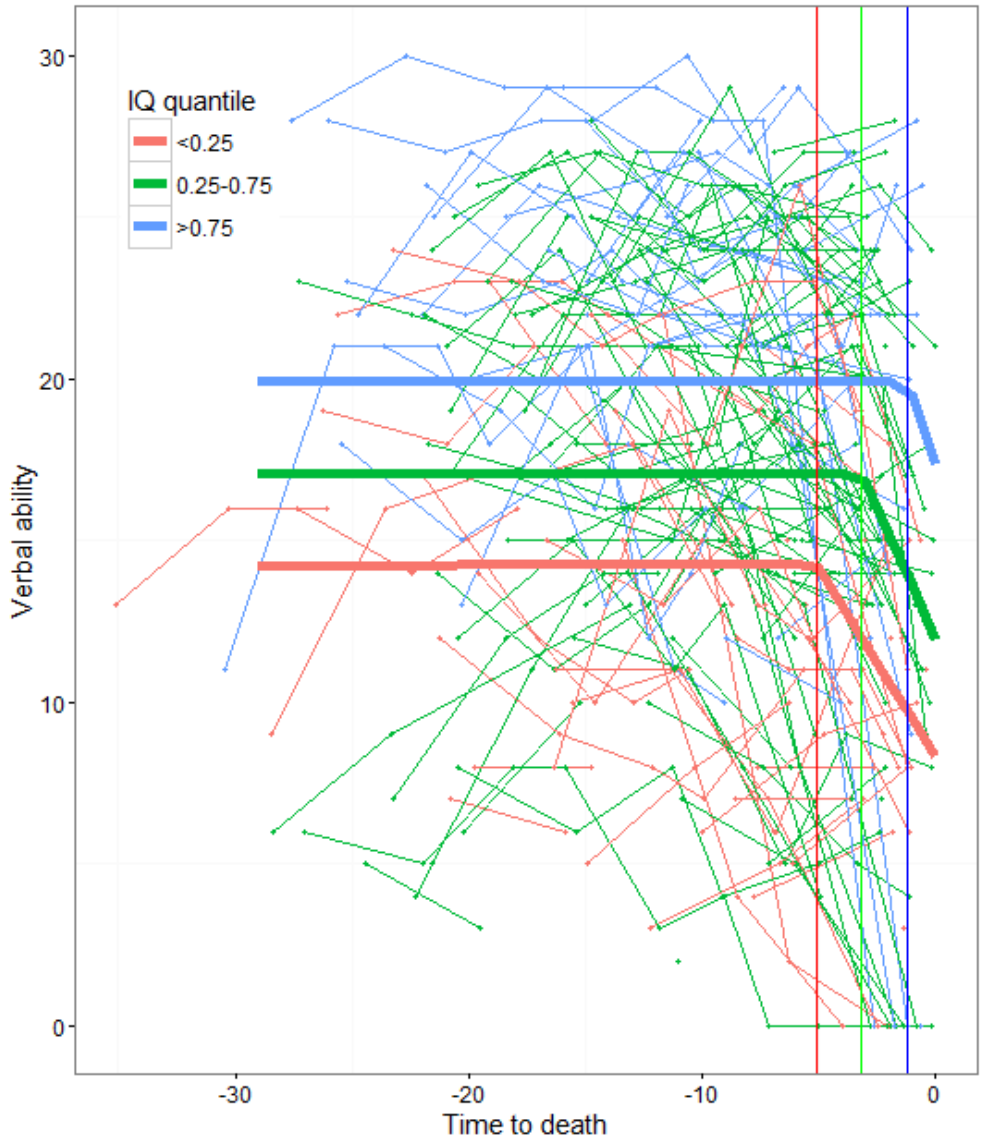
IQ quantile
<0.25
0.25-0.75
>0.75
Verbal ability
30
20
10
0
-30
-20
-10
0
Time to death

Figure 3c