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I forgot when I lost my grip - Strong associations between cognition and grip strength in level of performance and change across time in relation to impending death

Marcus Praetorius Björk*, **Boo Johansson**, and **Linda B. Hassing**
Department of Psychology, University of Gothenburg, Sweden

Abstract

An association between level of cognitive function and grip strength is well established while evidence for longitudinal associations of change in the two functions are still unclear. We examined associations between cognition and grip strength in levels of performance and in longitudinal change in late life in a population-based sample, aged 80 years and older at baseline, followed until death. The sample consisted of 449 non-demented individuals drawn from the OCTO-twin study. A test battery assessing 6 cognitive domains and grip strength was administered at five occasions with measurements intervals of two years. We fitted time to death bivariate growth curve models, adjusted for age, education and sex which resulted in associations between grip strength and cognition in both levels of performance (across all cognitive domains) and rates of change (in four out of six domains). These results show that cognition and grip strength change conjointly in later life and that the association between cognition and grip strength is stronger prior to death than earlier in life.

In the present study we further investigate the nature of the association between cognition and grip strength. More specifically we examine whether these two bio-behavioural functions change conjointly prior to death.

Baltes and Lindenberger (1997) suggested that the associations between cognitive performance and sensory function in later life share a common cause (i.e. a third factor) that drives the relationship where the third factor reflects general brain aging. In a similar vein, Christensen et al. (2001) explored the common cause hypothesis of cognitive aging were they found support for a common factor involved in performance in a range of physical and cognitive functions, among others grip strength. More recent studies have examined the relationship between cognition and grip strength in later life (Closuston et al., 2013; Deary et al., 2011; Sternäng et al., 2015). Both functions decline in later life (Singh-Manoux, et al., 2012; Sternäng et al., 2014), and have been shown to be related to health and subsequent mortality (Cooper et al., 2011; Cooper, Kuh, & Hardy, 2010; Leong et a., 2015; Small, Dixon, & McArdle, 2011). However, the nature of the observed association is not yet fully

*Corresponding author: Marcus Praetorius, MD, Department of Psychology, University of Gothenburg, Box 500, SE-405 30 Gothenburg, Sweden, +46 31 786-1646 (voice), Marcus.Praetorius@psy.gu.se.

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understood. Although there is clear evidence of associations between cognition and grip strength in level of performance the evidence for longitudinal associations are still unclear (Clouston et al., 2013).

In a systematic review and meta-analysis on the relationship between global cognitive function and physical function, Clouston et al., (2013) found small (β = 0.14; CI 95: β = 0.06 to β = 0.27) but consistent associations between level of cognitive performance and level of grip strength. One conclusion of the review, related to methodological concerns, was that despite a large number of longitudinal studies on the association between cognition and grip strength, few studies investigated if cognition and grip strength change conjointly. Only two longitudinal studies have examined the associations of simultaneous change in cognition and grip strength in a multi-wave design (i.e. ≥ 3 waves; see Deary et al., 2011; Sternäng et al., 2015). Deary et al., (2011) investigated trajectories of change in associations between fluid ability and grip strength. They confirmed a relationship between level of fluid ability and level of grip strength ($r = .20$), but found no evidence that fluid ability and grip strength share similar trajectories of change, a conclusion that does not lend support to the common cause hypothesis. On the other hand, Sternäng et al. (2015), examined change in cognition as a function of chronological age and a function of change in grip strength using time-variant covariant models (Sternäng et al., 2015). Their findings even suggest that change in grip strength preceded change in several cognitive domains (verbal ability, spatial ability, processing speed, and memory), an association that became more evident after age of 65 years, with effects ranging from β = 0.006 to β = 0.012.

The finding of more substantial association among older adults may relate to the terminal cognitive decline hypothesis (Kleemeier, 1962; Riegel & Riegel, 1972) which assumes that decline in cognitive functioning accelerates prior to death and that individual differences in cognitive change in later life are more strongly related to distance to death than to chronological age (Siegler, 1975). Several studies have confirmed that trajectories of cognition (Muniz-Terrera et al., 2013; Piccinin, Muniz, Matthews, & Johansson, 2011; Wilson, Segawa, Hizel, Boyle, & Bennett, 2012) and grip strength (Wilson, Segawa, Hizel, Boyle, & Bennett, 2012) are related to impending death (i.e. terminal decline). But no previous study has, to our knowledge, investigated potential associations between change in cognition and change in grip strength in relation to impending death. Thus, given that impending death reflects underlying global biological aging, it is of significance to examine if change in cognition is related to change in grip strength prior to death.

In the present study, we examine if cognition and grip strength changes conjointly prior to death, by conducting bivariate growth curve models (e.g. Deary et al., 2011). This is tested in very old individuals, without severe cognitive impairment (i.e., dementia), by using information from up to five assessments of both grip strength and multiple tests tapping several cognitive domains (i.e., semantic memory, episodic memory, spatial ability, motor- and perceptual speed, short-term memory and working memory). Given that both cognition and grip strength are related to mortality and decline in old age, we expect significant associations of shared common variability of change between cognition and grip strength and that these associations will be profound in this terminal phase of life.

Methods

Participants

Data was drawn from the OCTO Twin Study (McClearn et al., 1997) including a Swedish population-based twin sample, aged 80 years and older, born in 1893–1913, where both twins were alive at inclusion (N = 702 individuals/351 pairs). All participants were informed about the study in accordance with the ethics committee of the Karolinska Institute, the Swedish Data Inspection Board, and the institutional board at the University of Southern California or the Pennsylvania State University. Participants were examined five times at two year intervals in between 1991–2002. All examinations were conducted by registered nurses in the participant's place of residency with a broad based behavioral test battery. Test sessions took 3.5–4 hours, including rest periods. Individuals with dementia (n = 233) and individuals still alive at the time of the present study (n = 20) were excluded in the present analyses. After exclusions, 449 participants remained.

Measures

Ten tests were used to measure cognitive performance; the tests represent the domains of semantic memory, episodic memory, spatial ability, motor- and perceptual speed, short-term memory and working memory. The domains of semantic memory, episodic memory and spatial ability included more than one test. For these domains, we constructed factor scores using regression scores of each factor at each measurement.

Semantic memory—The Information test measures general knowledge and is a modified version (Jonson & Molander, 1964) of the Wechsler Adult Intelligence Scale, WAIS (Wechsler, 1981). Maximum score is 44 points. The Synonyms test requires the participant to find a synonym to match a target word; the task taps knowledge of verbal ability and is a part of the Dureman-Sälde battery (Dureman & Sälde, 1959).

Episodic memory—The Memory-in-Reality (MIR) test first requires the naming of 10 common real-life objects shown to the subject. The subjects are then instructed to place these objects in the different rooms of a three-dimensional model of an apartment, according to their own preferences. Thirty minutes later they are asked to recall the objects followed by a recognition task for the objects not recalled. Subjects are then asked to place the objects in the same locations as they did previously - the relocation test. The maximum score in each subtest is 10 (Johansson, 1988/1989). The present study only uses the recall subtest. Prose Recall is a Swedish prose recall task similar to the prose passages in the Wechsler Memory Test (WMS) (Wechsler, 1945). To maintain attention during presentation of the story, it was designed to be brief (100 words) and to have a humorous point. Subjects are asked to recall the story after presentation. Responses are coded for the amount of information recalled in a manner similar to the WMS. The maximum score is 16. Thurstone's Picture Memory is a nonverbal, long-term memory test (Thurstone & Thurstone, 1949). Subjects are shown 28 pictures and then asked for recognition of these among others distractors. The pictures were enlarged from the original version to minimize any possible visual problems. The maximum score is 28.

Spatial ability—Block Design requires reproduction of a pattern shown on a set of cards using red and white blocks and has a maximum score of 42. The Figure Logic task requires the person to identify one figure out of five in a row that is different in concept from the rest. Maximum score is 30. Both are part of the DS battery (Dureman & Sälde, 1959).

Motor- and perceptual speed—A modified version of the speeded Digit–Symbol Substitution Test (Wechsler, 1991) was used which measures motor speed and accuracy. The participant is given a list of symbols associated with digits from 1 to 9 and is asked to fill in the blanks with the symbols that correspond to each number. The test score is the total number of correct sequential matching of digits to symbols in a 90 seconds interval.

Short-term memory—The Digit Span forward Test measures short-term memory for orally presented digits (Wechsler, 1991). The subjects are asked to recall the digits in the same order as they were presented. The maximum score is 9.

Working memory—The Digit Span backward Test measures working memory for orally presented digits (Wechsler, 1991). The subjects are asked to recall the digits in reverse order. The maximum score is 8 for the backward part of the test.

Grip strength—Grip strength was measured by having participants squeeze a Martin vigorimeter (Elmed Inc., Addison, IL, USA; medium size bulb) three times for each hand, with the final score being the maximum force (in pounds per square inch) exerted in the 6 trials.

Age and education—Chronological age at first measurement occasion, gender and education were included in the analyses. Education was defined as total years of education. The educational level in our sample is low but typical for a Swedish cohort born in the late 1800 and early 1900.

Statistical analyses

First, we analyzed individual differences in levels and rates of linear and quadratic change in cognition and grip strength using hierarchical linear models (i.e., growth curve models) with repeated measure (i.e., time) nested within individuals nested within twin-pair (using TYPE=COMPLEX with CLUSTER which takes into account the non-independence of observations due to the cluster sampling of twin data (Muthén & Muthén, 1998–2010)). All models used maximum likelihood for the estimation of model parameters. This type of estimation is robust against a missing at random missing data assumption (Little & Rubin, 1987). Mplus uses full information maximum likelihood (FIML) estimator (Enders, 2006) in the presence of missing values. With FIML, parameters are estimated directly from the available raw data on a case-wise basis, and the $\chi 2$ test statistic and model fit indices are calculated from the log likelihood of the data for each observation (Duncan et al., 2006; Enders, 2006). The FIML procedure uses all available information to compute parameters (i.e., both partially complete and fully complete cases are used in the estimation), so that cases with partially missing data on the study variables can still be used in the analysis. Robust maximum likelihood (MLR) estimation was used given the clustered data (Muthén &

Muthén, 1998–2010). The MLR estimator, which is robust to non-normality by providing adjusted $\chi 2$ and standard errors, was used.

We specified the time factors as one year linear effects of “time to death” and centered intercepts at two years prior to death. The reason for centering the slope two years prior to death and not at the actual time of death was because it would not be possible to obtain performance score at this point. The slope was coded using negative values counting down to death. To exemplify, if a participant was examined at 10, 8, 6, 4 and 2 years before death the centered slope was coded as −8, −6, −4, −2 and 0.

Thereafter, we conducted bivariate growth curve models (e.g. Deary et al., 2011; Robitaille et al., 2012). The bivariate growth curve is a bivariate extension of the univariate latent growth curve with a latent growth process for each variable, including a group trend (fixed effects) and inter-individual differences (random effects) around this group trend. In the bivariate growth curve model, we analyzed two bivariate developmental relationships: (1) correlation among the intercepts, and (2) correlation among the slopes, i.e. (1) is the level of cognition prior to death related to the level of grip strength prior to death? (2) Is the amount of change in cognition related to the amount of change in grip strength? All models were controlled for age at first measurement occasion, education and gender (for background characteristics, see Table 1). Mplus 5.21 was used for analyses.

Results

First, we conducted analyses confirming the presence of longitudinal terminal change by conducting time to death growth curve models separately for each of the cognitive domains (episodic memory, semantic memory, short-term memory, spatial ability and motor- and perceptual speed) and grip strength. There were significant terminal decline in all outcomes (see Table 2).

Next, with purpose of investigating potential associations of levels of performance and rates of change between cognition and grip strength we conducted bivariate growth curve models with correlated intercepts and slopes. These models showed associations between level of performance in cognition with level of performance in grip strength across all cognitive outcomes (see Table 3; Model 1): semantic memory ($r = .31$), episodic memory ($r = .33$), spatial ability ($r = .47$), motor- and perceptual speed ($r = .41$), short-term memory ($r = .19$) and working memory ($r = .26$). This reflects that level of performance in cognition is related to level of performance in grip strength across all six cognitive domains prior to death.

There were associations between rates of change in cognitive performance and rates of change in grip strength across four out of six cognitive domains: semantic memory ($r = .49$), episodic memory ($r = .59$), spatial ability ($r = .78$) and short-term memory ($r = .38$; $p = .056$). This shows that the trajectories of cognitive performance were related to the trajectory of grip strength in four out of six cognitive domains, i.e. steeper terminal rate of change in semantic memory, episodic memory, spatial ability and short-term memory were associated with a steeper terminal rate of change in grip strength.

Discussion

In the present study we examined associations between cognition and grip strength in terms of level of performance and rates of change prior to death. Pertaining to associations in level of performance, we found significant associations between level of cognitive function and level of grip strength across all cognitive domains. Concerning associations between changes in performance, we found significant associations between change in grip strength and change in four out of six cognitive domains, that is, in semantic memory, episodic memory, spatial ability and short-term memory.

Our results of associations in levels of performance were expected and in line with findings from several other studies (e.g. Aichberger et al., 2010; Clouston et al., 2013; Deary et al., 2011; Kuh et al., 2009). In comparison to other findings our results are to be considered as relatively strong in terms of effect sizes. A systematic review and meta-analysis (Clouston et al., 2013) reported effect sizes of .14 for the association of level of global cognition and level of grip strength and effect sizes of .05 for the association of level of fluid ability and level of grip strength. In other words, our effect sizes regarding similar level of performance are larger across all cognitive domains (i.e. ranging from $r = .19$ in short-term memory to $r = .47$ in spatial ability). This is in line with our hypothesis that the association between level of cognition and level of grip strength is strengthened and more profound in very old ages (i.e. prior to death).

However, some of the cognitive tasks in the OCTO-twin test battery are partly dependent on motor functions while the other tests were performed orally which could have influenced the results of associations between level of cognitive performance and level of grip strength. The strongest associations between level of cognition and level of grip strength were found in the cognitive domains where the tasks involve motor functions (i.e. spatial ability and motor-and perceptual speed) which strengthen this assumption.

Regarding, our results of associations between rates of change in cognition and rate of change in grip strength we found significant associations of conjointly rate of change between cognition and grip strength in four out of six cognitive domains, i.e. in semantic memory, episodic memory, spatial ability and short-term memory. The effect sizes for these associations ranged from $r = .38$ (short-term memory) to $r = .78$ (spatial ability). The results showed no significant associations of similar rate of change in motor- and perceptual speed and working memory with rate of change in grip strength. Notable, the direction of the association, even so non-significant, between rate of change in working memory and rate of change in grip strength was negative. This reflects that decline in working memory is associated with an increase in grip strength. Our results indicate that the association of conjointly rate of change between cognition and grip strength in later life are explicit in to specific cognitive domains rather than cognitive performance in general.

There are only two studies that have tested if cognition and grip strength changes together in later life in a multi-wave design with mixed results (Deary et al., 2011; Sternäng, 2015). Deary et al., (2011), found no support for that fluid ability and grip strength changes together in later life (i.e. mean age of 79 years of age). Even if we used the same modelling approach (BLCM) in a similar age cohort (80 +) we used different time metrics, i.e. Deary et al, (2011), modelled change as time in study while the present study modelled change using an intra-individual time to death time estimate. A methodological challenge in longitudinal studies on cognitive aging is how to handle the survival effect that results in that longitudinal data will eventually consist of a more selected group of healthy survivors, who live longer, perform better, and decline less on cognitive tests. Modelling change as time to death will better estimate for the survival effects in longitudinal data, in comparison to other time metrics such as modelling time as chronological age or as time in study. Further, several studies also demonstrate that individual differences in cognitive change in later life reflect distance to death rather than chronological age (e.g. Siegler, 1975; Thorvaldsson, Hofer, & Johansson, 2006). Our results further indicate that also the association between rate of change in cognitive performance and rate of change in grip strength in later life is stronger prior to death in comparison to increasing chronological age (e.g. see Deary et al., 2011). Another possible explanation for the different results in the present study in comparison to Deary et al., (2011) is that they only used a single test of fluid ability (i.e. Raven's Standard Progressive Matrices). As previous mentioned, the present study found associations of parallel change in cognitive performance and grip strength in four out of six tests which indicate that the association of rate of change in cognition and rate of change in grip strength may be explicit in specific cognitive domains and it is possible that a broader range of cognitive outcomes would have resulted in different conclusions from Deary et al., (2011) regarding conjointly change between cognitive performance and grip strength in later life. In the systematic review and meta-analyses by Clouston et al., (2013) the authors also argue for the need of future studies with a broader range of cognitive tasks to better describe the nature of the developmental associations between cognition and grip strength in later life (see Clouston et al., 2013).

Further, Sternäng et al., (2015) showed that change in grip strength preceded change in cognitive performance. They found small (from $\beta = 0.006$ to $\beta = 0.012$) but consistent effects across four different cognitive domains (i.e. verbal ability, spatial ability, processing speed, and memory), with effects that became more pronounced after 65 years of age. In comparison, the association of similar rates of change in cognition and grip strength that was found in present study was substantially stronger which indicates that developmental associations of change between cognitive performance and grip strength are even more pronounced in later life, which may also to some extent explain the findings, of stronger effects after 65 years of age, that was found in Sternäng et al., (2015).

There are three potential explanations of the association of similar change in cognition and grip strength. One is that change in cognition drives change in grip strength. Another explanation is that change in grip strength drives change in cognition. The third explanation, and what we have tested in the present study, is that cognition and grip strength share similar variability of change. However, this implicates that a third factor (i.e. a shared common cause) impacts change in cognition and grip strength. This shared common cause is most possibly an effect of general brain aging (e.g. see Baltes & Lindenberger, 1997 and Christensen et al., 2001), that affects both cognition and grip strength. In the present study, we investigated associations between cognitive performance and grip strength in “normally ageing” individuals by only including individuals without a diagnosis of dementia. We should however bear in mind that at this very old age (i.e. 80 + years with about 7 years of survival), many of the individuals are most likely to be affected by dementia neuropathology to some extent also after adjusting for diagnoses of dementia. This could partly explain the overall large developmental associations between cognitive performance and grip strength that were demonstrated in the present study.

The present study had some strength that should be highlighted. Especially the opportunity to model cognitive- and grip strength change trajectories conditioned on mortality status, across a broad battery covering several cognitive domains across multiple waves in a population-based sample.

However, the study also had a few limitations that needs to be recognized. One was that some cognitive domains were only measured with a single test marker which might limit reliability in our inference to the specific domains (i.e. motor- and perceptual speed, short-term memory and working memory). Another potential weakness regards to the analyses of the data. As seen in Table 2, several domains showed an accelerated decline prior to death. However, even if it is doable, it is complicated to interpret the relationship between two developmental processes using BLCM when the quadratic functional forms are modelled. We therefore, only used linear models in the present analyses. Accelerated cognitive and grip strength decline prior to death are nonetheless interesting and can have implications for the association between cognitive performance and grip strength in later life. In case of that future studies chose to also examine this type of developmental associations, alternative linear models with for example two linear components, such as piecewise models, are therefore to recommend (see more detailed discussion about this in e.g. Robitaille et al., 2012).

In sum, our findings demonstrate that there are associations of level of performance and change between cognition and grip strength in later life. The overall large associations between cognitive performance and grip strength, in comparison to previous findings, points out that developmental association between cognitive performance and grip strength are most pronounced in very old ages.

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Table 1

Background Characteristics of the Sample across the Study Period

	T1	T2	T3	T4	T5
N	**449**	**397**	**272**	**201**	**155**
Time to death, *M (SD)*	6.88 (4.37)	5.94 (3.93)	5.29 (3.57)	4.53 (2.82)	3.41 (2.48)
Age, *M (SD)*	83.52 (3.23)	85.46 (3.12)	87.12 (2.77)	88.92 (2.78)	90.69 (2.39)
Education, *M (SD)*	7.30 (2.50)	7.30 (2.50)	7.30 (2.50)	7.30 (2.50)	7.30 (2.50)
Female, %	64.4	64.7	65.1	71.1	72.9

Table 2

Estimated Level and Rate of Decline in Cognition and Grip Strength as a Function of Time to Death

	Semantic memory		**Episodic memory**		**Spatial ability**		**Speed**		**Short-term memory**		**Working memory**		**Grip strength**	
	β	***SE***	**β**	***SE***	**β**	***SE***	**β**	***SE***	**β**	***SE***	**β**	***SE***	**β**	***SE***
Level of performance	49.81	0.52	49.46	0.52	49.15	0.47	48.72	0.47	50.61	0.38	49.78	0.42	48.85	0.50
Rate of change	−0.77	0.10	−0.98	0.12	−1.20	0.12	−0.73	0.11	−0.53	0.12	−0.67	0.14	−0.91	0.11
Change in rate of change	−0.05	0.01	−0.05	0.01	−0.07	0.01	−0.05	0.01	−0.03	0.01	−0.03	0.01	−0.07	0.01

Note: All estimations of levels and rates of decline in cognition and grip strength where significant given a CI 95 %.

Table 3

Correlations of Level of Performance and Change in Cognition and Grip strength prior to death

	Grip strength		
Cognitive performance	***r***	***SE***	***p***
Semantic memory			
Level of performance[a]	.31	0.06	<.001
Rate of change[b]	.49	0.18	.005
Episodic memory			
Level of performance	.33	0.07	<.001
Rate of change	.59	0.21	.006
Spatial ability			
Level of performance	.47	0.06	<.001
Rate of change	.78	0.25	.002
Motor- and perceptual speed			
Level of performance	.41	0.08	<.001
Rate of change	.30	0.34	.372
Short-term memory			
Level of performance	.19	0.08	.017
Rate of change	.38	0.20	.056
Working memory			
Level of performance	.26	0.08	.001
Rate of change	−.30	0.43	.480

Note:

[a]Cross-domain correlation between level of performance;

[b]Cross-domain correlation between average rate of linear decline; Means and regression coefficients from the models are not presented in the table.