right @ 2021 American Academy of Neurology

Copyright © 2021 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

Improved Cognitive Function in the Tromsø Study in Norway From 2001 to 2016

Bente Johnsen, MD, Bjørn Heine Strand, PhD, leva Martinaityte, MD, PhD, Ellisiv B. Mathiesen, MD, PhD, and Henrik Schirmer, MD, PhD

Neurology: Clinical Practice December 2021 vol. 11 no. 6 e856-e866 doi:10.1212/CPJ.00000000001115

Abstract

RESEARCH

Background and Objectives

Physical capacity and cardiovascular risk profiles seem to be improving in the population. Cognition has been improving due to a birth cohort effect, but evidence is conflicting on whether this improvement remains in the latest decades and what is causing the changes in our population older than 60 years. We aimed to investigate birth cohort differences in cognition.

Methods The study comprised 9,514 participants from the Tromsø Study, an ongoing longitudinal cohort study. Participants were aged 60–87 years, born between 1914 and 1956. They did 4 cognitive tests in 3 waves during 2001–2016. Linear regression was applied and adjusted for age

cohort study. Participants were aged 60–87 years, born between 1914 and 1956. They did 4 cognitive tests in 3 waves during 2001–2016. Linear regression was applied and adjusted for age, education, blood pressure, smoking, hypercholesterolemia, stroke, heart attack, depression, diabetes, physical activity, alcohol use, BMI, and height.

Results

Cognitive test scores were better in later-born birth cohorts for all age groups, and in both sexes, compared with earlier-born cohorts. Increased education, physical activity, alcohol intake, decreasing smoking prevalence, and increasing height were associated with one-third of this improvement across birth cohorts in women and one-half of the improvement in men.

Discussion

Cognitive results were better in more recent-born birth cohorts compared with earlier born, assessed at the same age. The improvement was present in all cognitive domains, suggesting an overall improvement in cognitive performance. The 80-year-olds assessed in 2015–2016 performed like 60-year-olds assessed in 2001. The improved scores were associated with increased education level, increase in modest drinking frequency, increased physical activity, and, for men, smoking cessation and increased height.

The Western population is getting older, and in Norway, the population older than 70 years is estimated to increase from 12% today to 21% in 2060.¹ It is well documented that aging is the largest risk factor for cognitive decline. Cognitive function has improved over the last century in the general adult population, a trend known as the Flynn effect.² However, a negative Flynn effect has been reported in the latest decades of the twentieth century,³ suggesting that a plateau for the improvement has been reached. The improvement in cognition is probably a cohort effect, commenced by multifactorial change in the population on factors influencing the brain and its function.⁴



Correspondence

bente.johnsen@unn.no

Dr. Johnsen

Department of Clinical Medicine (BJ, IM, EBM, HS), UIT The Arctic University of Norway; Department of Medicine (BJ, IM), University Hospital of North Norway, Tromsø; Norwegian Institute of Public Health (BHS), Oslo; Department of Neurology (EBM), University Hospital of North Norway, Tromsø; Department of Cardiology (HS), Akershus University Hospital, Lørenskog; and Institute of Clinical Medicine (HS), University of Oslo, Norway.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Modifiable risk factors for cognitive decline have been identified.⁵⁻⁹ Among these factors, education seems to be the most promising protecting factor for cognitive decline.^{4,5} The population-based Tromsø Study in Norway has gathered a broad range of multidisciplinary health information from the adult population of Tromsø for five decades. The study has found improvement in cardiovascular risk factor profiles^{10,11} and biomarkers of aging such as physical capasity measured by grip strength.¹² Therefore, we aimed to determine whether cognition has improved in later-born cohorts of older adults assessed 15 years apart. If so, which factors have contributed the most to this improvement?

Methods

The Tromsø Study is the longest-running Norwegian ongoing population-based longitudinal cohort study, with repeated screening of inhabitants in the municipality Tromsø, Norway.¹³ Seven surveys (Tromsø 1–7) have been conducted since 1974. Participants were recruited based on the national registry data of adult inhabitants. Each survey included both new individuals and individuals who had participated before, based on a complex sampling design described elsewhere.^{13,14} Cognitive testing was introduced in Tromsø 5 and repeated in Tromsø 6 and Tromsø 7.¹³⁻¹⁵ The present study includes Tromsø 5–7 (Table 1 and Figure 1). Participants who had taken part in the second part of Tromsø 4 in 1994/95 and a random sample of participants attending for the first time¹⁴ were eligible for invitations to the second visit in Tromsø 5-7. For the second visit in Tromsø 5, 85% of those eligible attended (n = 5,939), in Tromsø 6, 64% (n = 7,350), and in Tromsø 7, 60% (n = 7,804).¹⁶ Participants aged 60–88 years who had completed at least 1 cognitive test (n = 9,514, 54.4% women) in Tromsø 5–7 were eligible for the present study. Of these, 6,034 had participated once, 2,708 twice, and 782 in all 3 surveys with 7 or 14-15 years apart. Those attending only Tromsø 5 had a higher mean age (Tromsø 5: 71.8 years; Tromsø 6: 65.9 years; and Tromsø 7: 65.2 years) and a higher percentage of participants with only primary education (85.7%) compared with those who participated only in Tromsø 7 (30.1%) and those participating in all 3 surveys (66%). Those only attending Tromsø 5 also reported less physical activity. They had a higher frequency of smokers, people with high blood pressure and hypercholesterolemia, but not more depression. (Table 2 and eTable 1, links.lww.com/CPJ/A301).

Participants were stratified in 7-year birth cohorts and 7-year age bands to prevent overlapping birth cohorts, as Tromsø 5–7 were performed 7 years apart. The age-specific analyses were performed in 4 age bands: 60–66, 67–73, 74–80, and 80–87 years.

The Mini-Mental State Examination (MMSE) was excluded from the analyses as it was first introduced in 2008, and we aimed to explore trends since 2001. We, however, did 2 MMSE sensitivity tests: first excluding participants with MMSE scores of 19 or lower (n = 10 in Tromsø 6 and n = 34 in Tromsø 7)

Table 1	Birth Cohorts	and Age	Bands by	Tromsø Study
	Wave			

	Tromsø 5, year 2001	Tromsø 6, year 2007/8	Tromsø 7, year 2015/16		
Birth cohort	Age, y (n total)	Age, y (n total/ n new)	Age, y (n total/ n new)		
1914–1920	81–87 (115)				
1921-1927	74–80 (1,076)	81-87 (307/38)			
1928-1934	67–73 (1,506)	74–80 (806/90)	81-87 (247/14)		
1935-1941	60–66 (1,600)	67–73 (1,230/202)	74–80 (959/134)		
1942-1948		60–66 (1,788/1,788)	67–73 (1,995/804)		
1949-1955			60–66 (2,157/2,157)		
Total	4,297	4,131	5,358		

and second excluding participants with MMSE 20–24 (n = 141 in Tromsø 6, n = 397 in Tromsø 7), to check for impact of participants with probable neurodegenerative disease.

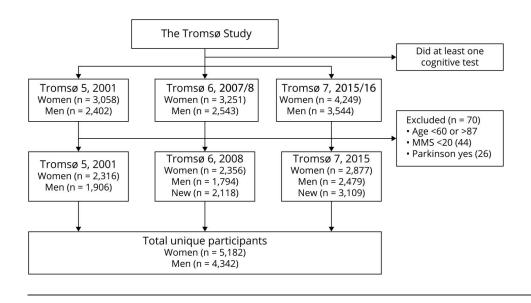
Measurements of Cognitive Function

Word test 1 (WT1) is a 12-word memory test of short-term verbal memory.⁶ The participants were given 2 minutes to complete a free immediate recall of 12 nouns that were shown written on a board and read aloud at 5-second intervals. One point was given for correct recall of each word. Scores ranged from 0 to 12.^{17,18} Word test 2 (WT2) is a test of long-term verbal memory, episodic memory, and the ability to use learning strategies.⁶ The 12 words from WT1 were shown and read aloud again mixed with 12 new nouns. The participants were asked to identify each word as new or known. One point was given for each correctly identified word. Points ranged from 0 to 24.17,18 The digit symbol coding test (DSCT) is part of the Wechsler Adult Intelligence Scale.¹⁹ It is used to examine perceptual processing, perceptual motor speed, and memory²⁰ and is sensitive enough to reveal small changes in cognition, as it is influenced by psychomotor ability, sustained attention, processing speed, episodic memory, and executive function.⁹ This test pairs 9 numbers with 9 symbols. Participants were asked to fill in as many correct symbols in numbered blank squares as they could in 90 seconds without skipping a square. The number of correct symbols was the score of the test.^{6,21} In the finger-tapping test (FTT), a test measuring psychomotor speed,²² the participants tapped their nondominant index finger on a button for four 10-second rounds. The result was the mean tapping count of the last 3 rounds.

Risk Factors for Cognitive Decline, Possibly Affecting Cohort Differences

We chose factors that are proposed as detrimental or beneficial for cognitive function: education, high blood pressure, smoking hypercholesterolemia, stroke, alcohol consumption, diabetes, depression, heart attack, physical activity, height, and body mass





index (BMI).^{5,6,23-25} Height is an indicator of nutrition early in life and health care.²⁶ Participants filled out questionnaires on life style. For details, see eAppendix 1 (links.lww.com/CPJ/A301).

Statistical Analyses

Data from all study waves were pooled and analyzed as 1 set. First, to investigate whether cognitive test scores improved in later-birth cohorts, we performed a multiple linear regression analysis in each of the age bands, with the respective cognitive tests as the dependent variable and study wave as the independent covariate. All models were adjusted by age and sex. Second, to investigate how much other covariates mediated the changes in test scores between study waves, covariates were added one by one in the whole age span (in the following order: age, education, blood pressure, hypercholesterolemia, smoking, stroke, previous heart attack, depression, diabetes, physical activity, alcohol units, alcohol frequency, height, and BMI), and we investigated the change in percent in the coefficient for the study wave. The interaction terms age × study waves and study wave × sex and sex × age and sex \times age \times study wave were included to allow for different changes over time by sex and age. We used Stata 14.2. There were 2,852 missing values in one or more of the covariates, which were adjusted with multiple imputation by chained equation. The imputation was based on the variables age, sex, and study wave and the respective cognitive variable. The cognitive test scores were not imputed. All missing values of the mediators were below 3.5%, except for alcohol consumption (n = 2,707), depression (n = 2,707)= 1,099), and physical activity. Physical activity in Tromsø 5 had a high missing rate (n = 2,852), as the participants older than 70 years (n = 1,615) were asked a different question.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was funded by Northern Norway Regional Health Authority (Helse Nord RHF). The Regional Committee for Medical and Health Research Ethics approved the study (REK Nord, reference 2016/389). Written informed consent was given by all participants.

Data Availability

Data cannot be made public as legal restrictions are set by the Tromsø Study Data and Publication Committee. Researchers can apply for data access at uit.no/research/tromsostudy/project?pid=709148.

Results

The mean age of the participants was 68.8 years, with the range 60–87 years and interquartile range 63–73. Description of participants can be found in Table 2. Education levels in the Tromsø municipality have increased markedly over the last century (eFigure 1, links.lww.com/CPJ/A301). We found an increase over time in people drinking alcohol 2 or more times per week, but they did not increase the amount of alcohol per occasion. Later-born participants reported more leisure exercise and smoking prevalence declined over time, especially in men. Rates of hypercholesterolemia decreased, and participants had better controlled blood pressure. There was a minor increase in BMI and diabetes, but little change in number of other comorbid conditions.

Scores in all 4 cognitive tests improved in later-born birth cohorts for all age bands, in both sexes by 5%–51% compared with earlier born tested at the same age (Table 3). The greatest improvement was seen in DSCT and the least in WT2.

Women scored better on short-term memory, long-term verbal and episodic memory, visuospatial function, perceptual motor speed, and sustained attention (WT1, WT2, and DSCT)

Copyright © 2021 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

\ge	60-66				67-73			74–80				81-87				
Survey year	2001	2007/8	2015/16		2001	2007/8	2015/16		2001	2007/8	2015/16		2001	2007/8	2015/16	
Birth cohort	1935–1941	1942-1948	1949-1955	<i>p</i> Value	1928-1934	1935-1941	1942-1948	p Value	1921-1927	1928-1934	1935-1941	<i>p</i> Value	1914-1920	1921-1927	1928-1934	<i>p</i> Valu
Vomen																
n	897	1,138	1,123		774	638	1,064		617	395	485		65	131	114	
Mean height, cm	168	163	164	<0.001	166	161	162	<0.001	165	160	160	<0.001	163	158	158	0.06
Low education, %	82	66	29	<0.001	85	78	45	<0.001	92	85	55	<0.001	89	88	63	<0.00
Smoking, yes %	28	20	16	<0.001	24	17	11	<0.001	16	15	8	<0.001	11	6	7	0.323
Inactive, %	15	19	11	<0.001	14	18	13	<0.001	NA	28	17	<0.001	NA	40	20	0.00
Alcohol, %				<0.001				<0.001				<0.001				< 0.00
Teetotaler	12	13	7		17	22	12		26	31	23		21	50	29	
Monthly or less	50	30	23		57	36	28		55	38	34		62	30	37	
2–4 times/month	28	33	37		18	25	33		12	22	25		10	13	22	
2–3 times/week	8	17	27		7	13	20		5	8	11		7	4	9	
4≤ times/week	2	7	6		1	4	8		2	2	7		0	4	4	
5≤ units/occasion	0.7	1.0	1.1	0.538	0.5	0.6	0.5	0.948	0.5	0.2	0.2	0.640	0	0.5	0.8	0.788
7≤ units/occasion	0.1	0.2	0	0.348	0.5	0	0	0.01	0.2	0	0.2	0.680	0	0.5	0	0.581
Hypertension, %	48	44	30	<0.001	62	60	45	<0.001	68	68	59	0.002	77	75	71	0.576
High cholesterol, %	92	84	82	<0.001	91	81	77	<0.001	93	79	74	<0.001	94	79	70	<0.001
Depression, %	3.6	3.5	3.6	0.990	2.4	2.3	2.3	0.978	1.8	2.6	1.3	0.369	4.6	4.4	1.5	0.332
Heart attack, %	2.2	2.1	1.8	0.771	5.5	6.2	2.0	<0.001	8.1	8.4	5.1	0.088	17.2	9.9	4.5	0.014
Diabetes, %	4.0	4.2	5.5	0.186	4.6	8.9	7.9	0.003	7.2	7.0	9.1	0.409	6.3	10.9	9.5	0.663
BMI mean	26.9	27.4	26.7	0.003	26.9	26.9	27.7	<0.001	27.2	27.1	26.9	0.556	26.8	27.2	26.8	0.678
/len																
n	697	801	1,010		718	539	881		453	325	405		50	92	106	
Mean height, cm	168	177	177	<0.001	167	175	176	<0.001	166	173	174	<0.001	165	172	173	<0.001
Low education, %	71	53	24	<0.001	78	65	32	<0.001	82	70	36	<0.001	80	79	42	<0.001

Neurology.org/CP

e859

60-66 67-73 74-80 81-87 2001 2007/8 2015/16 2001 2007/8 2015/16 2001 2007/8 2015/16 2001 2007/8 2015/16 1935-1941 1942-1948 1949–1955 *p* Value 1928–1934 1935–1941 1942–1948 p Value 1921–1927 1928-1934 1935–1941 *p* Value 1914–1920 1921–1927 1928-1934 7 8 7 Smoking, yes % 27 17 14 < 0.001 26 16 11 < 0.001 17 14 < 0.001 6 17 17 12 < 0.001 14 15 15 <0.001 NA 21 15 0.017 NA 22 17 < 0.001 < 0.001 < 0.001 3 4 5 5 11 5 6 15 11 6 30 14 Monthly or less 40 26 17 50 32 21 58 34 30 67 38 38 37 29 33 39 20 33 32 17 27 2-4 times/month 36 39 16 2-3 times/week 16 23 32 11 17 24 10 15 18 4 6 15 4 8 9 4 8 5 3 9 6 9 6 4≤ times/week 11 7.5 0.306 3.9 0.995 2.6 0.665 0 5≤ units/occasion 7.9 9.4 3.8 3.9 2.6 1.8 0.8 1.8 0.419 1.0 0.206 0.4 0.193 0 0 7≤ units/occasion 1.2 1.6 2 0.2 0.6 0.8 0 0 Hypertension, % 53 52 35 < 0.001 55 54 42 < 0.001 66 62 49 < 0.001 60 63 54 High cholesterol, % 85 73 64 < 0.001 80 65 57 < 0.001 80 59 47 < 0.001 84 53 42 Depression, % 1.2 0.8 1.9 0.132 1.5 1.9 0.4 0.025 2.4 2.7 0.4 0.031 2.0 0.8 1.8 Heart attack, % 11.6 7.2 6.7 0.001 15.0 15.2 9.9 0.002 19.2 22.4 11.7 < 0.001 20.8 21.9 13.2 0.324 5.3 0.003 6.0 0.003 10.6 5.4 6.9 7.1 8.9 9.9 7.7 11.9 8.3 6.7

p Value

0.02

0.123

< 0.001

0.561

0.332

< 0.001 0.758

0.198

0.702

0.005

Abbreviation: BMI = body mass index.

27.0

27.7

27.8

< 0.001 26.4

27.2

Low education: primary up to 10 years; inactive: low physical activity on leisure time; hypertension: systolic blood pressure >140 and/or diastolic blood pressure >90; cholesterol >5 mmol/L; depression is reported for last week. p Values obtained by x-square test for categorical variables and 1-way analysis of variance for continuous variables.

< 0.001 26.3

26.7

27.4

< 0.001 25.0

26.6

26.9

27.9

Table 3 Cognitive Crude Mean Scores at Tromsø 5 and Tromsø 7 and Difference in Regression Coefficient in Adjusted Models

			Difference in cognition								
		Mean crude test score at T7	Model 1			Model 2					
Age	Mean crude test score at T5		Change in cognition regression βT5–βT7	95% Cl marked with <i>p</i> value	% Change cognition regression βT5-βT7	Change in cognition regression βT5–βT7	95% Cl marked with <i>p</i> value	% Change cognition regression βT5-βT7			
Vord test 1	, number im	mediately r	ecalled 0–12								
Women											
60-66	6.70	7.64	0.9	0.8 to 1.1***	16.1	0.5	0.3 to 0.7***	7.9			
67-73	6.06	7.04	1.0	0.8 to 1.1***	17.5	0.5	0.4 to 0.7***	9.9			
74-80	5.47	6.37	0.9	0.7 to 1.1***	18.0	0.6	0.3 to 0.8***	10.6			
81-87	4.85	5.38	1.1	0.6 to 1.7***	25.1	1.0	0.4 to 1.5**	17.5			
Men											
60-66	6.38	7.19	0.8	0.6 to 0 0.9***	13.4	0.3	0.1 to 0.5**	6			
67-73	5.66	6.51	0.8	0.7 to 1.0***	17.6	0.4	0.2 to 0.6***	10.9			
74-80	5.18	5.96	0.8	0.5 to 1.0***	17.1	0.3	0.0 to 0.6**	9.1			
81-87	4.73	5.59	0.9	0.3 to 1.5**	19.5	0.5	-0.2 to 1.2	6.6			
Nord test 2	, recognition	of words 0	-24								
Women											
60-66	21.45	22.48	1.0	0.8 to 1.2***	9.9	0.7	0.5 to 0.9***	3.6			
67-73	20.75	22.21	1.4	1.2 to 1.7***	7.6	1.1	0.9 to 1.3***	5.9			
74-80	20.40	21.62	1.2	0.9 to 1.5***	6.6	0.9	0.5 to 1.2***	4.4			
81-87	20.09	21.47	1.6	0.7 to 2.6**	9.8	1.6	0.6 to 2.6**	8.2			
Men											
60-66	21.18	22.19	1.0	0.8 to 1.2***	5	0.6	0.4 to 0.9***	3.5			
67-73	20.62	21.88	1.3	1.0 to 1.5***	6.7	0.9	0.7 to 1.2***	5.2			
74-80	20.35	21.29	0.9	0.6 to 1.3***	5.2	0.7	0.3 to 1.1***	4			
81-87	20.45	21.46	1.0	0.1 to 1.9*	5.2	0.3	-0.7 to 1.3	2.6			
Digit symbo	ol coding, sur	n correct sy	mbols in 90 s								
Women											
60-66	34.84	45.54	10.5	9.5 to 11.4***	33.3	7.2	6.2 to 8.1***	22.5			
67-73	28.77	39.92	11.0	10.0 to 12.0***	42.9	7.8	6.8 to 8.6***	30.7			
74-80	24.54	33.08	8.6	7.4 to 9.6***	38.8	5.8	4.6 to 7.0***	26.4			
81-87	20.21	26.86	7.3	4.0 to 10.6***	41.1	6.1	2.9 to 9.3***	31			
Men											
60-66	33.7	41.09	6.9	5.8 to 7.9***	22.7	3.8	2.5 to 4.6***	12.7			
67-73	27.38	36.81	9.3	8.3 to 10.2***	38.2	6.0	5.0 to 7.0***	25.1			
74-80	23.51	30.90	7.3	5.9 to 8.8***	37.8	4.2	2.7 to 5.7***	22.3			

Neurology.org/CP

Neurology: Clinical Practice | Volume 11, Number 6 | December 2021

Copyright © 2021 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

e861

Continued

 Table 3
 Cognitive Crude Mean Scores at Tromsø 5 and Tromsø 7 and Difference in Regression Coefficient in Adjusted

 Models (continued)
 Models (continued)

			Difference in co	gnition					
			Model 1			Model 2			
Age	Mean crude test score at T5	Mean crude test score at T7	Change in cognition regression βT5-βT7	95% Cl marked with <i>p</i> value	% Change cognition regression βT5-βT7	Change in cognition regression βT5-βT7	95% Cl marked with <i>p</i> value	% Change cognition regressior βT5–βT7	
81-87	22.5	25.94	3.9	0.5 to 7.3*	17	1.3	-1.9 to 4.5	4.7	
inger tapp	ing test, sum	tapped no	ndominant finge	er 10 s					
Women									
60-66	48.59	52.17	3.4	2.7 to 4.2***	8.5	2.0	1.2 to 2.8***	5	
67-73	45.32	48.30	2.9	2.1 to 3.7***	8.6	1.3	0.4 to 2.2**	4.5	
74-80	41.26	46.56	5.3	4.1 to 6.5***	15.9	3.7	2.4 to 5.0***	10.7	
81-87	38.57	44.12	6.5	3.1 to 9.9***	26.3	5.2	1.6 to 8.8**	20.4	
Men									
60-66	53.68	57.01	3.1	2.2 to 3.9***	7.5	1.3	0.3 to 2.2**	4.6	
67-73	49.95	52.75	2.7	1.8 to 3.5***	7.6	1.3	0.3 to 2.2**	4.4	
74-80	45.81	49.71	3.9	2.5 to 5.2***	11.1	2.5	1.1 to 4.0**	7.8	
81-87	45.89	47.85	1.6	-2.0 to 5.1	4.2	-0.9	-4.6 to 2.9	-2.3	

Age- and sex-specific multiple linear regression model, testing the change in cognitive score for each age group. Age groups are nonoverlapping. This means that participants are never in the same age group twice. Model 1: adjusted for age. Tromsø 5 and Tromsø 7 are used as independent variables. Model 2: model 1 + education, blood pressure, hypercholesterolemia, smoking, previous stroke, previous heart attack, diabetes, depression, activity, alcohol consumption, height, and body mass index. Change in β-Tromsø 7 is reported, and percentage change for the β-coefficient adjusted for both models. Mean values are crude means in age group for given survey. Percentage change is calculated by the regression coefficient of the logarithmic values for the cognitive test in given age group and sex, adjusted for model 1 and model 2. *p* Values are marked as follows: *p < 0.05, **p < 0.01, ***p < 0.001.

compared with men (Table 3 and Figure 2). They also had higher age-specific improvement than men did over time (interaction for sex by study wave: p < 0.05 for all 3 cognitive tests). For psychomotor speed (FTT), however, the sex difference was reversed, with higher scores and larger improvement over time for men than for women. In DSCT, men improved more than women at older age ($\Delta\beta = 0.1$), and the opposite for the FTT, on which women improved more at older age ($\Delta\beta = 0.02$). On the FTT, older women had larger improvement over time in cognitive test scores than the younger women (p = 0.008), whereas for DSCT, younger women improved the most.

When adjusted for all included mediators, the cognitive test score improvements in later-born were still statistically significant, except in the oldest men (Table 3), indicating other factors mediating the improvement in the younger age bands. The most prominent mediator for improved cognitive scores in later-born birth cohorts was education. When the early-born and most recent born birth cohorts were compared, education mediated 40.6% of the improvement in female WT1 scores and 52.9% in male scores. It was less, but still a substantial mediator for the improvement on WT2, mediating more than 20% for both sexes. Education was mediating 19.9% in women and 31.3% in men, of the improvement on the DSCT results,

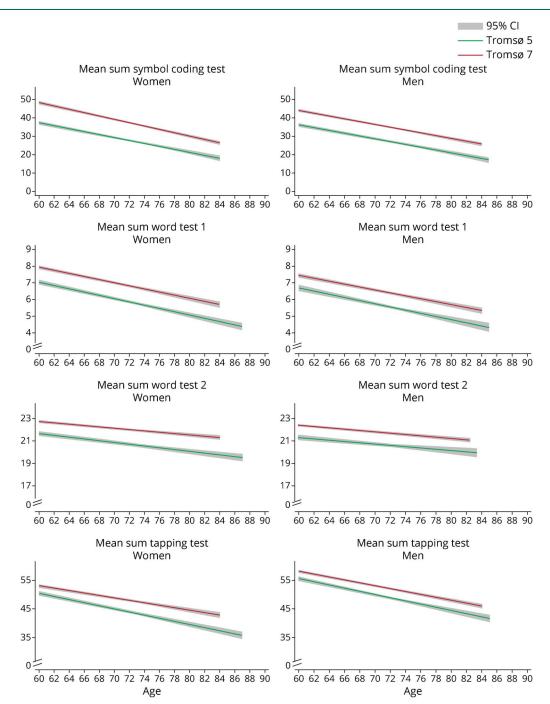
whereas the results of FTT scores improved by 29.4% and 35.3% in women and men, respectively.

Increase in alcohol drinking frequency mediated 24.9% of the improvement in FTT score in women and 17.6% in men. For WT1, it mediated 23% of the improvement in women and 19.5% in men. Within each occasion, the effect of increasing consumption had a weak (0.6% or less) negative trend on all cognitive tests, equal for both sexes. Reporting more than 5 units of alcohol per occasion, was for men associated with decreasing test performance on DSCT and FTT. (men p < 0.01, women p > 0.05).

Increased physical activity was associated with improved test scores, especially in short-term memory and psychomotor speed, with a mediating effect of 4.2%–6.8% on cognitive outcomes.

Among men, less smoking in later-born birth cohorts mediated 12.2% of the improvement in the FTT and 9.3% of improvement in WT1, whereas in women, smoking was not a mediator. Increased height in later-born cohorts was associated with 21.3% of the improvement in WT1 in men and 7.6% in women. Conjointly, increased education, physical activity, alcohol intake, height and decreased smoking

Copyright © 2021 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.



Estimation is done with linear regression with 95% confidence interval (CI). The y-axis has scale brake for WT1, WT2 and FTT to better illustrate the age-specific improvement over time.

prevalence in later-born birth cohorts, mediated on average 34.4% (range 24.5%–47.7%) of the improvement in women's results on the 4 cognitive tests. Men's average improvement in the 4 cognitive tests on the same conjoined factors was 51.6% (range 35.8–73.4%).

We performed sensitivity tests excluding those having had a stroke, with no substantial difference in the results. We also excluded participants with Parkinson disease and all those with MMSE scores of 19 or below with no substantial difference in results. Excluding those with MMSE <25 from Tromsø 6 and Tromsø 7, enlarged improvement in cognitive scores as MMSE was not performed in Tromsø 5 (n = 581), the reference group. However, after removing those testing in the lower areas on MMSE in T6 and T7, the covariates had less influence on the change, with largest effect on short time memory (eTables 2–4 links.lww.com/ CPJ/A301).

Discussion

In this large population-based study, we found improvement in cognitive test scores in more recently born birth cohorts. The scale of these differences varied in the 4 cognitive tests, but on the DSCT, the improvement corresponded to 12 years for women and 10 years for men, meaning that 70- to 72-year-olds in 2015/16 performed as 60-year-olds did in 2001. For WT1, the improvement was 10 years for both sexes, and for WT2, the test score improvement in was corresponding 20 years for both sexes, meaning that for recognition, 80 is the new 60 (Figure 2).

These positive associations were evident in all age bands and in both sexes represented in all 4 cognitive tests, covering different areas of cognition. The strongest mediating factors associated with improved cognition in more recent born birth cohorts were higher education levels, increased height, and smoking cessation for men and increased physical activity for both sexes. Higher cognitive test scores in those reporting more frequent, but yet moderate alcohol consumption was also observed.

Education was the most prominent mediator in the shortterm memory test (WT1), suggesting that education may benefit short-term memory. Our results confirm the findings of similar studies in other Western countries where educational levels have improved in the last century.²⁷⁻³¹ Also in this study's population, education levels have changed immensely over the last century in both sexes (Table 2 and eFigure 1, links.lww.com/CPJ/A301). This indicates that education improves not only resilience to damage and cognitive reserve capacity but also cognition in those without manifest neurodegenerative disease.

Psychomotor speed also improved over birth cohorts. This supports the possible relationship between the improvement in cognition and the improved physical strength shown in earlier studies¹² and the weak association between cardiovascular risk factors and cognition.²⁷

In the Tromsø Study, alcohol units per occasion did not change much from 2001 to 2015, but the frequency of occasions consuming alcohol increased. Excessive alcohol use is a well-known risk factor for cognitive decline.³² Studies have shown a J-shaped association between cognitive capacity and alcohol, suggesting a protective effect of moderate consumption and damage to the brain with excessive use.^{23,32} A study from 2010 using data from the Tromsø Study suggested improved cognition with increasing wine intake within a moderate range. As alcohol consumption increases with income and educational level, the authors thought that their findings were due to residual confounding factors, despite adjustment for education.³³ Another study confirmed the findings, but explained the improvement in cognitive performance to be related to sex differences, as women drank more wine and men drank more beer and

liquor, and women outperformed men in cognitive tests.⁴ A cutoff at 21 >units per week has been suggested as a risk factor for dementia,⁵ and a large meta-analysis concluded that people older than 60 years increased their dementia risks with more than 2 times per week.³⁴ The majority of the population in the Tromsø Study were at or below the advocated limit for harmful drinking^{5,34} (Table 2). The moderately increased frequency of alcohol consumption in this study, however, was still strongly associated with the improved score on cognitive tests for both sexes. Confounding of not measured factors could be a possible explanation for this contradictory epidemiologic effect. Moderate alcohol consumption is also associated with higher education.^{5,6} With increasing years of education, a higher cognitive capacity could make brains more resilient to the damaging effects of alcohol. Moderate alcohol consumption is also linked with being socially active,³⁵ and frequency of consuming alcohol could be a confounder marking social interactions. Using abstainers as the reference group could introduce a selection bias, as abstainers in some studies have shown poorer health compared with moderate consumers.³⁶

Our analysis showed that physical activity was positively associated with cognitive test scores over birth cohorts, with a larger effect in men. It is recommended for people to be physically active to reduce the risk of cognitive decline.^{37,38} Previous studies in the Tromsø Study, with 7 years between analyzed waves, have also found low physical activity to be associated with lower scores in cognitive testing, but only in women.⁶ The positive effect of exercise in men in our study could be due to longer time of 14/15 years between the survey waves and a higher mean age. Our findings also comply with the same study on smoking, which had an inverse association with cognition in both sexes, and improvement in other cardiovascular risk factors such as hypertension and hypercholesterolemia to be only weakly associated with cognitive test scores.

With a large population of almost 10,000 people evaluated with 4 different cognitive tests covering different areas of cognition, and showing the same trends, the results are robust. The high attendance rate of 65% or higher in all 3 surveys ensures generalizability.¹⁶

The study included few excessive alcohol users and few with extreme obesity. It was not possible to make a variable for unit alcohol per week. This would have made the alcohol findings more comparable to the international literature. Participants were not asked about financial income in all survey waves.

In repeated testing, there could be introduced a learning bias. Reports on the subject are dissimilar. Some report an improved IQ score by 5–6 points²; others report a learning bias with mean test-retest interval of 47 days.¹⁸ With longer test-retest intervals of mean 370 days, 1 study reports that

Copyright © 2021 American Academy of Neurology. Unauthorized reproduction of this article is prohibited.

TAKE-HOME POINTS

- → Later-born birth cohorts have better score on cognitive tests compared with earlier born in a population aged 60–87 years.
- → In cognitive domains such as psychomotor ability, sustained attention, processing speed, episodic memory, and executive function, the improvement corresponded to 12 years for women and 10 years for men, indicating 70- to 72-year-olds in 2015/16 performed as 60-year-olds did in 2001.
- → For short-term memory, the improvement was 10 years for both sexes. For long-term verbal memory, episodic memory, and the ability to use learning strategies, the test score improvement corresponded to 20 years for both sexes, indicating that for these domains, 80 is the new 60.
- The improvement was positively associated with increased education level, increased drinking frequency, increased physical activity, and, for men, smoking cessation and increased height.

reliability improved in a geriatric population.¹⁷ Accordingly, we assume that the learning bias in our study, for the 37% that were tested more than once, will be very small as there is 15 years between testing.

Cognitive test scores were improved in the more recent born birth cohorts in all ages and in both sexes. The scale of these differences varied, but for some cognitive areas, 80 is the new 60. The improvement is positively associated with increased education level, increase in drinking frequency, increased physical activity, and, for men, smoking cessation and increased height.

Study Funding

Northern Norway Regional Health Authority (Helse Nord RHF) grant number: HNF1407-18.

Disclosure

The authors report no disclosures relevant to the manuscript. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Publication History

Received by *Neurology: Clinical Practice* January 15, 2021. Accepted in final form May 21, 2021.

Appendix Authors

Name	Location	Contribution
Bente Johnsen, MD	Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø; Department of Medicine, University Hospital of North Norway, Tromsø	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
Bjørn Heine Strand, PhD	Norwegian Institute of Public Health, Oslo	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
leva Martinaityte, MD, PhD	Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø; Department of Medicine, University Hospital of North Norway, Tromsø	Drafting/revision of the manuscript for content, including medical writing for content, and analysis or interpretation of data
Ellisiv B. Mathiesen, MD, PhD	Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø; Department of Neurology, University Hospital of North Norway, Tromsø	Drafting/revision of the manuscript for content, including medical writing for content
Henrik Schirmer, MD, PhD	Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø; Department of Cardiology, Akershus University Hospital, Lørenskog, Norway; Institute of Clinical Medicine, University of Oslo, Norway	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

References

- Sentralbyrå S. Lavere Befolkningsvekst Framover. 2018. Accessed April 23, 2020. ssb. no/befolkning/artikler-og-publikasjoner/lavere-befolkningsvekst-framover
- Flynn JR. Massive IQ gains in 14 nations: what IQ tests really measure. Psychol Bull. 1987;101:171-191.
- Dutton E, van der Linden D, Lynn R. The negative Flynn effect: a systematic literature review. Intelligence. 2016;59:163-169.
- Corley J, Cox SR, Deary IJ. Healthy cognitive ageing in the Lothian Birth Cohort studies: marginal gains not magic bullet. *Psychol Med.* 2018;48(2):187-207.
- Livingston G. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020;396(10248):413-446.
- Arntzen KA, Schirmer H, Wilsgaard T, Mathiesen EB. Impact of cardiovascular risk factors on cognitive function: the Tromso study. *Eur J Neurol*. 2011;18(5):737-743.
- Mungas D, Gavett B, Fletcher E, Farias ST, DeCarli C, Reed B. Education amplifies brain atrophy effect on cognitive decline: implications for cognitive reserve. *Neurobiol Aging*. 2018;68:142-150.
- Sattler C, Toro P, Schonknecht P, Schroder J. Cognitive activity, education and socioeconomic status as preventive factors for mild cognitive impairment and Alzheimer's disease. *Psychiatry Res.* 2012;196(1):90-95.
- Hestad K, Engedal K, Schirmer H, Strand BH. The effect of blood pressure on cognitive performance. An 8-year follow-up of the Tromso study, comprising people aged 45-74 years. *Front Psychol.* 2020;11:607.
- Mannsverk J, Wilsgaard T, Mathiesen EB, et al. Trends in modifiable risk factors are associated with declining incidence of hospitalized and nonhospitalized acute coronary heart disease in a population. *Circulation*. 2016;133(1):74-81.
- Hopstock LA, Bonaa KH, Eggen AE, et al. Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: the Tromso study 1979 to 2008. *Hypertension*. 2015;66(3):496-501.
- 12. Strand BH, Bergland A, Jorgensen L, Schirmer H, Emaus N, Cooper R. Do more recent born generations of older adults have stronger grip? A comparison of three

cohorts of 66- to 84-year-olds in the Tromso study. J Gerontol A Biol Sci Med Sci. 2019; 74(4):528-533.

- Jacobsen BK, Eggen AE, Mathiesen EB, Wilsgaard T, Njolstad I. Cohort profile: the Tromso study. Int J Epidemiol. 2012;41(4):961-967.
- Eggen AE, Mathiesen EB, Wilsgaard T, Jacobsen BK, Njolstad I. The sixth survey of the Tromso Study (Tromso 6) in 2007-08: collaborative research in the interface between clinical medicine and epidemiology: study objectives, design, data collection procedures, and attendance in a multipurpose population-based health survey. *Scand J Public Health*. 2013;41(1):65-80.
- Lu K, Nicholas JM, Collins JD, et al. Cognition at age 70: life course predictors and associations with brain pathologies. *Neurology*. 2019;93(23):e2144-e56.
- Berrington de Gonzalez A, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. *New Engl J Med.* 2010;363(23):2211-2219.
- Woods SP, Scott JC, Conover E, et al. Test-retest reliability of component process variables within the Hopkins Verbal Learning Test-Revised. Assessment. 2005;12(1): 96-100.
- Benedict RHB, Schretlen D, Groninger L, Brandt J. Hopkins Verbal Learning Test—Revised: normative data and analysis of inter-form and test-retest reliability. *Clin Neuropsychol.* 2010;12(1):43-55.
- 19. Wechsler D. WAIS-IV: Wechsler Adult Intelligence Scale. Psychological Corp.; 2008.
- Joy S, Kaplan E, Fein D. Speed and memory in the WAIS-III Digit Symbol—Coding subtest across the adult lifespan. Arch Clin Neuropsychol. 2004;19(6):759-767.
- 21. Jaeger J. Digit symbol substitution test: the case for sensitivity over specificity in neuropsychological testing. *J Clin Psychopharmacol.* 2018;38(5):513-519.
- Roalf DR, Rupert P, Mechanic-Hamilton D, et al. Quantitative assessment of finger tapping characteristics in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease. J Neurol. 2018;265(6):1365-1375.
- Organization WH. Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. WHO; 2019.
- Baumgart M, Snyder HM, Carrillo MC, Fazio S, Kim H, Johns H. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a populationbased perspective. *Alzheimers Dement*. 2015;11(6):718-726.
- Fischer CE, Kortebi I, Karameh WK, et al. Examining the link between cardiovascular risk factors and neuropsychiatric symptoms in mild cognitive impairment and major depressive disorder in remission. J Alzheimers Dis. 2019;67(4): 1305-1311.

- Sundet J, Barlaug D, Torjussen T. The end of the Flynn effect? A study of secular trends in mean intelligence test scores of Norwegian conscripts during half a century. *Intelligence*. 2004;32(4):349-362.
- Thorvaldsson V, Karlsson P, Skoog J, Skoog J, Johansson B. Better cognition in new birth cohorts of 70 year olds, but greater decline thereafter. J Gerontol B Psychol Sci Soc Sci. 2017;72(1):16-24.
- Rönnlund M, Nilsson LG. The magnitude, generality, and determinants of Flynn effects on forms of declarative memory and visuospatial ability: time-sequential analyses of data from a Swedish cohort study. *Intelligence*. 2008;36(3):192-209.
- Christensen K, Thinggaard M, Oksuzyan A, et al. Physical and cognitive functioning of people older than 90 years: a comparison of two Danish cohorts born 10 years apart. *Lancet*. 2013;382(9903):1507-1513.
- Bancks M, Alonso A, Allen N, Yaffe K, Carnethon M. Temporal trends in cognitive function of older US adults associated with population changes in demographic and cardiovascular profiles. J Epidemiol Community Health. 2019;73(7):612-618.
- Munukka M, Koivunen K, von Bonsdorff M, et al. Birth cohort differences in cognitive performance in 75- and 80-year-olds: a comparison of two cohorts over 28 years. *Aging Clin Exp Res.* 2021;33(1):57-65.
- Sachdeva A, Chandra M, Choudhary M, Dayal P, Anand KS. Alcohol-related dementia and neurocognitive impairment: a review study. Int J High Risk Behav Addict. 2016; 5(3):e27976.
- Arntzen KA, Schirmer H, Wilsgaard T, Mathiesen EB. Moderate wine consumption is associated with better cognitive test results: a 7 year follow up of 5033 subjects in the Tromso Study. Acta Neurol Scand Suppl. 2010(190):23-29.
- Xu W, Wang H, Wan Y, et al. Alcohol consumption and dementia risk: a doseresponse meta-analysis of prospective studies. *Eur J Epidemiol*. 2017;32(1):31-42.
- Kelly S, Olanrewaju O, Cowan A, Brayne C, Lafortune L. Alcohol and older people: a systematic review of barriers, facilitators and context of drinking in older people and implications for intervention design. *PLoS One.* 2018;13(1):e0191189.
- Ormstad H, Rosness TA, Bergem AL, Bjertness E, Strand BH, Group G. Alcohol consumption in the elderly and risk of dementia related death—a Norwegian prospective study with a 17-year follow-up. *Int J Neurosci.* 2016;126(2):135-144.
- Mandolesi L, Polverino A, Montuori S, et al. Effects of physical exercise on cognitive functioning and wellbeing: biological and psychological benefits. *Front Psychol.* 2018;9:509.
- Morland C, Andersson KA, Haugen OP, et al. Exercise induces cerebral VEGF and angiogenesis via the lactate receptor HCAR1. *Nat Commun.* 2017;8:15557.