Cross-sectional associations between serum 25 hydroxyvitamin D and performance in three different cognitive domains among old adults

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2016

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Background

Have other studies shown an association between 25 hydroxyvitamin D and cognitive function?

- Studies have indicated an association between low levels of 25OHD and cognitive dysfunction in old age

Other studies criticized for…	AGES_Reykjavík (2002-2006)
Lack of adjustment	Number of covariates available
Small sample size (N< 250)	Large sample size (N= 5.764)
Limitation in choices of cognitive tasks	Multiple tests of cognitive function
Study population	Community-dwelling older adults

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Criticized for….

• Lack of adjustment
• Small sample sizes (N< 250)
• Limitation in the choices of cognitive tasks
• Heterogeneity in study population

What is known?

Vitamin deficiency/insufficiency high among old adults…

Higher risk in northern latitude…

Increased risk:
…low Physical activity
…high Body mass index

Vitamin D receptors located in brain…

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Background
-Cognitive decline-

Aging is generally known as a risk factor for cognitive decline and dementia.

The underlying mechanism are **multifactorial**, but the exact causes are still elusive.

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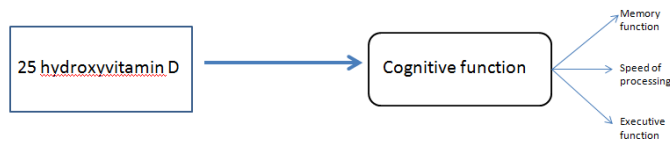
Vitamin D
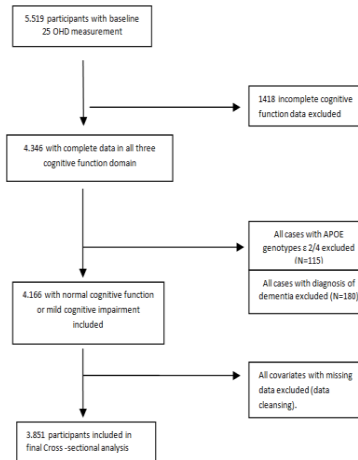
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Objective

Investigate the associations between serum 25OHD and cognitive function in a large population based cohort of old individuals living in Iceland.

25 hydroxyvitamin D → Cognitive function → Memory function
Speed of processing
Executive function

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Analytical sample

- Of the total (5.764)
- 5519 participants complete 25 OH D
- 4.346 complete Cognitive Function
- Dementia excluded (n=180, 3.1%)
- APOE$_4$ genotypes excluded (n=115, 2%)

5.519 participants with baseline 25 OHD measurement

1418 incomplete cognitive function data excluded

4.346 with complete data in all three cognitive function domain

All cases with APOE genotypes ε 2/4 excluded (N=115)

All cases with diagnosis of dementia excluded (N=180)

4.166 with normal cognitive function or mild cognitive impairment included

All covariates with missing data excluded (data cleansing).

3.851 participants included in final Cross -sectional analysis

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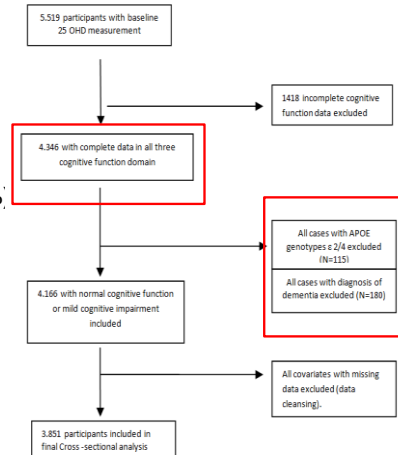
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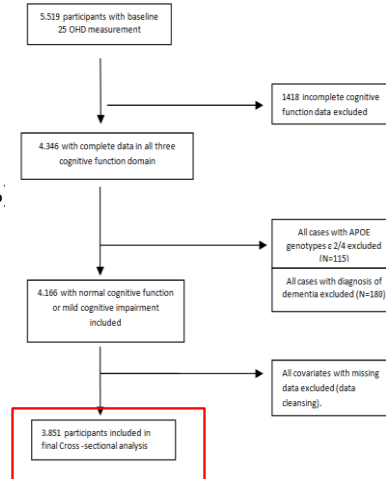3.851 participants included in final Cross -sectional analysis

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Methods

- Serum 25 hydroxyvitamin D (IHA laboratory)
  - Deficient (≤30 nmol/L) (REF.)
  - Insufficient (≥31-49 nmol/L)
  - Normal-high levels (≥50 nmol/L)
- Cognitive function assessment
  - Composite score for..
    - Memory performance
    - Speed of processing
    - Executive function

1. Raw scores were converted to standardized z scores

2. Each domain converted to low and high scores.

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Statistical analysis

- Logistic regressions were used and odds ratios calculated.
- Adjustment for confounding
  - Model 1: age, sex and education
  - Model 2: added
    - physical activity and body mass index
  - Model 3: added to model 2
    - medication use, diabetes, hypertension, depressive symptoms, alcohol consumption and smoking .

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Results
Part I

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**Baseline characteristics according to serum 25 hydroxyvitamin D concentrations in men and women.
The AGES-Reykjavik study 2002-2006.**

Mean, ± SD or %	25(OH) D		
	<30 nmol/L	31-49 nmol/L	≥50 nmol/L
(Number)	(957)	(1639)	(2923)
Age (years)	76.68±5.69	76.69±5.64	76.59±5.55
BMI (kg/m^2)	27.73±5.07	27.64±4.56	26.51±4.0**
Diabetes$^€$ (Yes/ no)	15.6	13.2	10.6***
Hypertension$^¥$ (Yes/ no)	84.5	81.3	79.6***
Education, elementary n (%)	228 (29.2)	225 (24.1)	580 (19.4)***
Geriatric depression score ≥6	7.7	6.3	5.0**
Demented (Yes/ no)	8.2	6.0	5.2***
Medication (≥5)	44.5	39.0	38.7**
Smoking (yes)	15.2	9.4	7.3***
Alcohol consumption (yes)	56.1	62.3	68.6***
Physical activity (≥3h/w)	8.9	27,7	63.4***
Memory function	-0.13±0.91	0.019±0.93	0.06±0.92***
Working memory	-0.14±0.70	-0.03±0.69	0.059±0.7***
Speed of processing	-0.15±0.87	-0.01±0.86	0.05±0.87***

Significance estimates for the comparison between 25(OH) D groups: * p< .05; ** p> .01; *** p> .001.
$^¥$Hypertensive : systolic BP > 140 mmHg, diastolic BP > 90 mmHg or on hypertensive medicine.
$^€$Diabetes mellitus was defined by physician's diagnosis of diabetes, use of diabetes medication and/or fasting blood glucose of >7.0 mmol/L.

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Mean scores on memory function, speed of processing and working memory according to 25 OHD
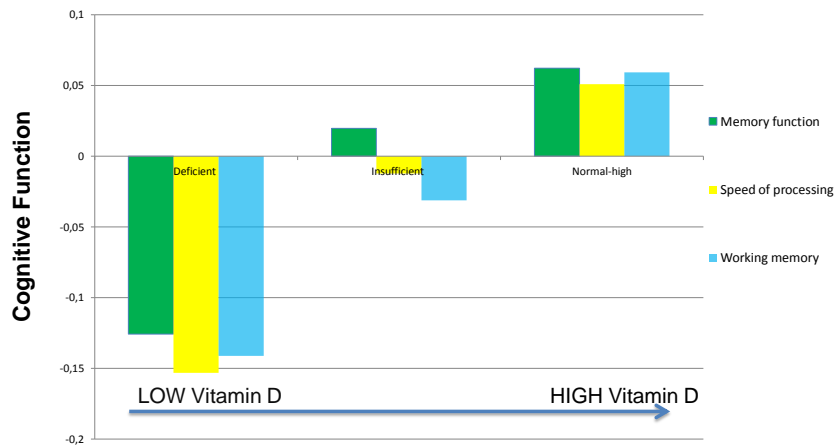
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RESULTS

Part II

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Odds ratio for higher scoring on speed of processing, memory function and executive function according to 3 levels of 25 hydroxyvitamin D.

	≤ 30 nmol/L	30-50 nmol/L	≥ 50nmol/L
	(Deficient)	*(Insufficient)*	*(Normal-High)*
Cognitive performance	OR (95% CI)	aOR (95% CI)	aOR (95% CI)
Speed of processing			
Model I	1.00 (ref.)	1.533 (1.255-1.873)	1.666 (1.386-2.004)
Model II	1.00	1.486 (1.216-1.817)	1.583 (1.314-1.907)
Model III	1.00	1.268 (1.033-1.558)	1.342 (1.107-1.626)
Memory function			
Model I	1.00 (ref.)	1.451 (1.191-1.769)	1.543 (1.286-1.851)
Model II	1.00	1.407 (1.153-1.716)	1.476 (1.227-1.776)
Model III	1.00	1.291 (1.055-1.580)	1.334 (1.104-1.611)
Executive function			
Model I	1.00 (ref.)	1.240 (1.013-1.519)	1.449 (1.203-1.746)
Model II	1.00	1.219 (0.995-1.493)	1.392 (1.153-1.680)
Model III	1.00	1.082 (0.895-1.359)	1.275 (1.050-1.547)

*Model I: Adjusted for age, gender, education

**Model II: Adjusted for age, gender, education, physical activity and body mass index

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Conclusion

- We found that 25OHD levels above >30 nmol/L and/or >50 nmol/L was associated with better cognitive function among community dwelling old adults as compared to 25OHD levels below <30 nmol/L.

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Thank you!

- Alfons Ramel
- Milan Chang
- Pálmi V. Jónsson
- Ólöf G. Geirsdóttir
- RHLÖ
- Colleagues and co-workers at RHLÖ

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Memory function
1 test

- Test used:
  - California Verbal Learning Test (CVLT).
    - 4 semantic categories
      - Fruits, clothes, tools and spices.
      - CVLT detected memory impairments
      - 16 words, 4 catagories, read 4 times (modified version).
        » Example of 1 category: Fruits (apples, bananas, oranges and cherries).

      - Test played from CD.

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Speed of processing

- Digit Symbol Substitution Test (DSST).
  - The DSST requires that the participant correctly pairs a series of symbols with the numbers 1 through 9.
  - Total time for the test is 90.

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Speed of processing

- Figure Comparision
  - The participant is required to compare two small figures and indicate whether they are similar or dissimilar, max 1 min per test. 30 sec per page.

- Stroop part I (Word reading black print)
  - The Stroop test appears sensitive to dementia
  - *Participant is asked to read given words as fast as possible*

- Stroop part II (colour naming)

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Executive function

- Digit Backward
  - Backward memory span is a more challenging variation which involves recalling items in reverse order. Digit-span task is used to measure working memory's number

- Shortened version of CANTAB spatial working memory test
  - touch-screen and acts as a training procedure to ensure that the sucbject can touch the screen accurately. It simultaneously screens for visual and movement problems ans ensures that the subject can hear, understand and follow simple instructions

- Stroop test part III
  - (Word colour interference)

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Now state the colors as fast as you can

Row 1	Red	Blue	Green	Yellow
Row 2	Yellow	Green	Blue	Red
Row 3	Green	Red	Yellow	Blue

From John Gosbee, MD, MS, VA National Center for Patient Safety