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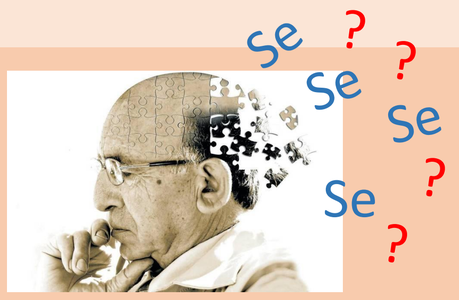
Selenium levels in patients with mild cognitive impairment and Alzheimer's disease



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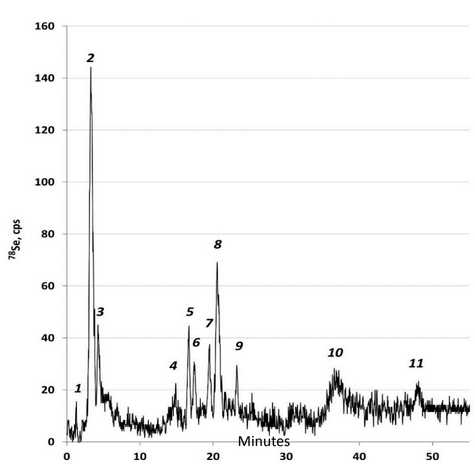
Background and aim

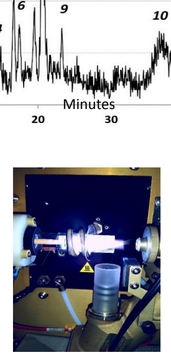
The exposure to neurotoxic trace elements has been implicated in the etiology of several neurologic diseases and some recent concern has focused the metalloid selenium (Se).

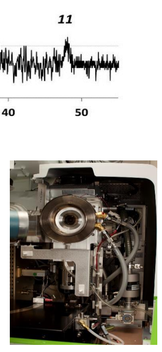
Se may exists in several chemical species with markedly different and even opposite biological properties and both excess or deficiency of Se has been linked to Alzheimer's disease.

In this study we sought to evaluate the different interpretations that could be carried out depending on the time of sampling of Se.



1 Injection peak
2 SePP
3 SeM
4 Unknown
5 GPx
6 SeC
7 TrxR
8 Se(IV)
9 Se-HSA1
10 Se-HSA2
11 Se (VI)





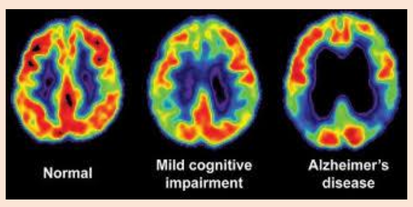
Methods

Within a prospective study design investigating the potential etiologic role of Se species in cerebrospinal fluid (CSF) and the progression to AD in persons with mild cognitive impairment (MCI), we compared Se levels in subjects with AD and subjects with MCI which evolved in AD during the follow-up.

Table 1. Baseline characteristics of study population

	AD		MCI			
			Converted to AD		Remaining MCI	
	N	%	N	%	N	%
All participants	33	100	21	100	29	100
Sex						
Males	16	48.5	10	47.6	17	58.6
Females	17	51.5	11	52.4	12	41.4
Age at entry						
<65 years	21	63.6	6	28.6	14	48.3
≥65 years	13	36.4	15	71.4	15	51.7
Education						
<8 years	6	18.2	5	28.8	11	37.9
8-12 years	12	36.4	8	38.1	8	27.6
≥13 years	15	45.4	8	38.1	10	34.5
APOE ε4						
Non-carriers	11	33.3	4	19.0	14	48.3
Carriers	14	42.4	9	42.9	8	27.6
Missing	8	24.3	8	38.1	7	24.1

Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment



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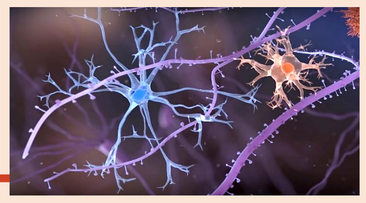
Results



CSF samples from 33 AD ('stable AD') and 50 MCI subjects were finally collected, and of these latter after a median follow-up of 42 months, 29 remained MCI ('stable MCI'), while 21 evolved to AD ('converted AD').

Our results showed that patients with pre-existing stable AD had lower levels of overall Se and inorganic Se in particular compared with stable MCI and converted AD, as baseline total Se CSF level were 4.08 (Interquartile range - IQR 3.72-4.56) in stable MCI, 4.40 (IQR 3.63-5.09) in converted AD and 3.68 (IQR 2.91-4.31) in stable AD and selenate (one of the main inorganic Se species) levels were 0.12 (IQR 0.09-0.31) in stable MCI, 0.23 (IQR 0.13-0.34) in converted AD and 0.12 (IQR 0.06-0.23) in stable AD.

Levels of organic species showed opposite results with 1.88 (IQR 1.28-2.27) in stable MCI, 1.60 (IQR 1.03-2.18) in converted AD and 1.84 (IQR1.19-2.25) in stable AD.

Table 2. Distribution of levels of Se species (μg/L) and of β-amyloid, total (t-tau) and phosphorylated (p-tau) tau proteins (pg/mL) in cerebrospinal fluid of the study population

	AD		MCI			
			Converted to AD		Remaining MCI	
	50th	IQR	50th	IQR	50th	IQR
Total Se	3.68	2.91 - 4.31	4.40	3.63 - 5.09	4.08	3.72 - 4.56
Inorganic Se	0.44	0.34 - 0.60	0.67	0.43 - 0.80	0.63	0.46 - 0.75
Se(IV)	0.34	0.24 - 0.42	0.40	0.30 - 0.62	0.41	0.34 - 0.57
Se(VI)	0.12	0.06 - 0.23	0.23	0.13 - 0.34	0.12	0.09 - 0.31
Organic Se	1.84	1.19 - 2.25	1.60	1.03 - 2.18	1.88	1.28 - 2.27
Se-SelenoP	1.52	0.84 - 1.91	1.45	0.94 - 1.83	1.63	1.20 - 2.04
Se-Met	0.18	0.10 - 0.23	0.15	0.07 - 0.23	0.13	0.08 - 0.22
Se-Cys	0.01	0.01 - 0.08	0.01	0.01 - 0.01	0.01	0.01 - 0.01
Se-GPX	0.05	0.01 - 0.12	0.01	0.01 - 0.06	0.01	0.01 - 0.09
Se-HSA	1.26	0.86 - 1.52	1.65	1.16 - 1.84	1.40	1.16 - 1.79
Unknown	0.12	0.04 - 0.36	0.28	0.16 - 0.47	0.25	0.14 - 0.36
β-amyloid	452	385 - 499	506	417 - 519	699	521 - 963
t-tau	597	440 - 791	625	404 - 743	256	198 - 404
p-tau	96	77 - 118	86	73 - 128	60	46 - 85

Abbreviations: AD, Alzheimer's disease; IQR, interquartile range; MCI, mild cognitive impairment; Se(IV), selenite; Se(VI), selenate; Se-SelenoP, selenoprotein P-bound Se; Se-Met, selenomethionine-bound Se; Se-Cys, selenocysteine-bound Se; Se-GPX, glutathione-peroxidase-bound Se; Se-HSA, human serum albumin selenium-bound Se.

Conclusions

Our results point out an opposite behavior of Se levels depending on both species considered and time of sampling.

That difference could explain such inconclusive results of previous case-controls studies that generally assessed Se levels after the onset of the disease, thus they could be hampered by the neuropathological modifications during the progression of the disease.

Therefore, our findings highlight the importance of considering both the type of Se species and the time of sampling in order to avoid misinterpretation of the etiologic role of this metalloid into the process leading to AD, especially when results come from non-prospective studies.

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