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Background

There is growing evidence that a high level of homocysteine (Hcy) is a risk factor for Alzheimer Disease (AD). It has been demonstrated that individuals with high-Hcy levels have lower gray matter thickness and volumes in several brain regions. There is evidence that behavioural symptoms in AD (BPSD) are positively correlated with Hcy plasma level. To our knowledge, the potential impact of high levels of Hcy in specific cognitive functions in AD has never been investigated.

Objective

To determine the influence of Hcy level on cognitive profile in AD.

Methods

323 patients with AD were enrolled in a prospective study; they underwent an extensive neuropsychological examination exploring many cognitive domains (memory, language, visuo-perception, visuospatial abilities, executive function, constructional praxis, ideomotor praxis). The effects of Hcy levels and of other risk factors (including cholesterol, smoking habits, triglycerides) were analysed.

Results

Generalized Liner Model showed a significant drop in performance with increasing Hcy that was highly specific for memory tests (of both verbal and visuo-spatial material, and on both short and long term recall) and for Lurias motor planning test; these were pure effects of Hcy as effects of all other predictors were partialled out.

	Expected direction of effect	MMSE	RAVEN	CORSI SPAN	DIGIT SPAN	REY FIGURE ST-RECALL	REY FIGURE LT-RECALL	REY LIST ST-RECALL	REY LIST LT-RECALL	SEMANTIC FLUENCY	PHONEMIC FLUENCY	NAMING	READING	COMPREHENSION	LURIA	OVERLAPPING FIGURES	REY FIGURE COPY	APRAXIA LEFT HAND	APRAXIA RIGHT HAND	STROOP COLOUR NAMING TIME
Gender		2,87						3,06			3,34	4,22				3,86				
Age	The older, the worse							3,87				1,75						-2,3	-1,4	
Education	The higher, the better	7,03	8,16	5,52	11,1	2,29	3,5	1,97		1,72	19,6	16,9	8,05	7,33	6,84	10,8	8,19	0,75	0,51	8,26
Duration	The longer, the worse	5,35				1,65	1,76		2,04									1,45	0,83	
Smoke	Smokers have lower performance																			
High Blood Pressure	The higher, the worse																			
Family History	+ : lower performance												8,52							
Glycemia	The higher, the worse																			
HDL-Col	The higher, the better			1,78																
LDL-Col	The higher, the worse												4,61							
TGL	The higher, the worse	-1,3																		2,28
Hcy	The higher, the worse	1,1				1,92	2,78	1,14	1,39						1,76					

Table - Effect sizes (Eta Squared = % of SS explained) are reported for significant effects. Significance was assessed at Alpha=0.05; this was one-tailed when an expected direction was available (see relevant column), two-tailed otherwise. When an effect was two-tailed significant in an unexpected direction, it was reported as a negative value. Gender: in all cases the significant effect meant an advantage of ladies over gentlemen.

Conclusion

We showed for the first time that high Hcy levels correlate with poor performance in long- and short- term spatial and verbal memory and with motor planning in AD. These results may support the hypothesis that Hcy has an impact on medial temporal and dorsal frontal areas, and are in line with neuroimaging studies showing reduced thickness of temporal cortex in patients with AD and hyperhomocysteinemia.

References

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