

SUPPLEMENTARY MATERIAL

The Supplementary Material includes:

Assessment of cognitive function in MCI and control groups.

Supplementary Tables S1-S4.

Supplementary Figures S1-S3.

Assessment of cognitive function in MCI and controls groups

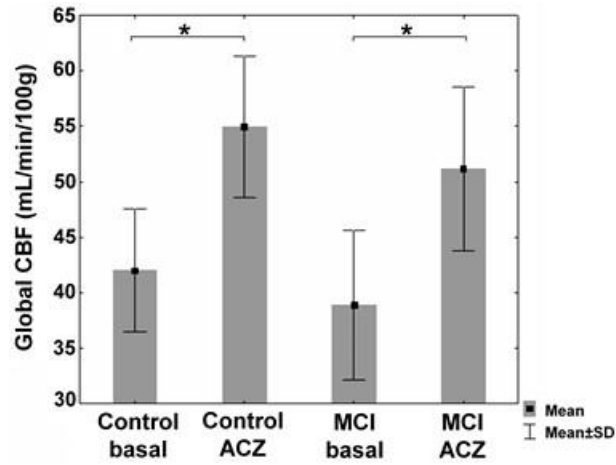
The cognitive function was assessed for each participant by a neuropsychological battery comprising mnemonic and nonmnemonic specific tests. Mnemonic tests included Rey Complex Figure test (delayed recall) for episodic memory assessment, logical memories A and B (immediate recall) and paired associate learning (easy and hard-word pairs, immediate recall) of the Wechsler memory scale (WMS). Nonmnemonic tests comprised the copy of the Rey Complex Figure test, attentive matrices [1], token test [2], verbal fluency [3], digit span of WMS (forward and backward items), and Trail Making A and B tests.

All mnemonic test scores, except easy-word pair learning, showed significant reduction in the MCI group as compared with control group (Supplementary Table I). In contrast, all nonmnemonic test scores showed no significant differences between groups.

Supplementary Table S1. Cognitive function in MCI and control groups

	MCI (N=26)	Control (N=26)	p value
<u>Mnemonic Tests</u>			
<i>Rey complex fig. (delayed recall)</i>	9.4 ± 4.8	18.1 ± 5.2	10 ⁻⁶
<i>Logical memory A</i>	9.9 ± 3.5	11.7 ± 3	0.02
<i>Logical memory B</i>	8.4 ± 3.4	10.2 ± 3.1	0.04
<i>Easy-word pair learning</i>	8.1 ± 1.3	8.6 ± 0.7	0.06
<i>Hard-word pair learning</i>	3 ± 2.4	5.7 ± 2.5	1.7 x 10 ⁻⁵
<u>Nonmnemonic Tests</u>			
<i>Rey complex fig. (copy)</i>	31 ± 5.5	32.7 ± 4.4	0.16
<i>Attentive matrices</i>	40.9 ± 10	44.9 ± 9.7	0.07
<i>Token test</i>	32.5 ± 3.1	33.5 ± 2	0.07
<i>Verbal fluency</i>	9.1 ± 3.6	10 ± 2.9	0.18
<i>Digit span (forward)</i>	5.6 ± 1.2	5.9 ± 1	0.16
<i>Digit span (backward)</i>	4.5 ± 0.8	4.9 ± 0.9	0.07
<i>Trail Making A</i>	42.7 ± 7.6	39.4 ± 4.7	0.08
<i>Trail Making B</i>	117.1 ± 22.2	107.9 ± 14.5	0.08

Data shown as mean ± S.D. Differences between groups were tested using ANCOVA, modeling group as a categorical independent variable and controlling for age, gender and level of education. Bonferroni was used as a post-hoc test.



Supplementary Figure S1. Global CBF in the control and MCI groups in the two conditions: basal and under the acetazolamide (ACZ) challenge. Both groups responded similarly to the ACZ challenge by significantly increasing the CBF compared to the basal condition (*- $p < 10^{-6}$).

Supplementary Table S2. Brain regions with significant CBF increase due to ACZ challenge in MCI and control groups.

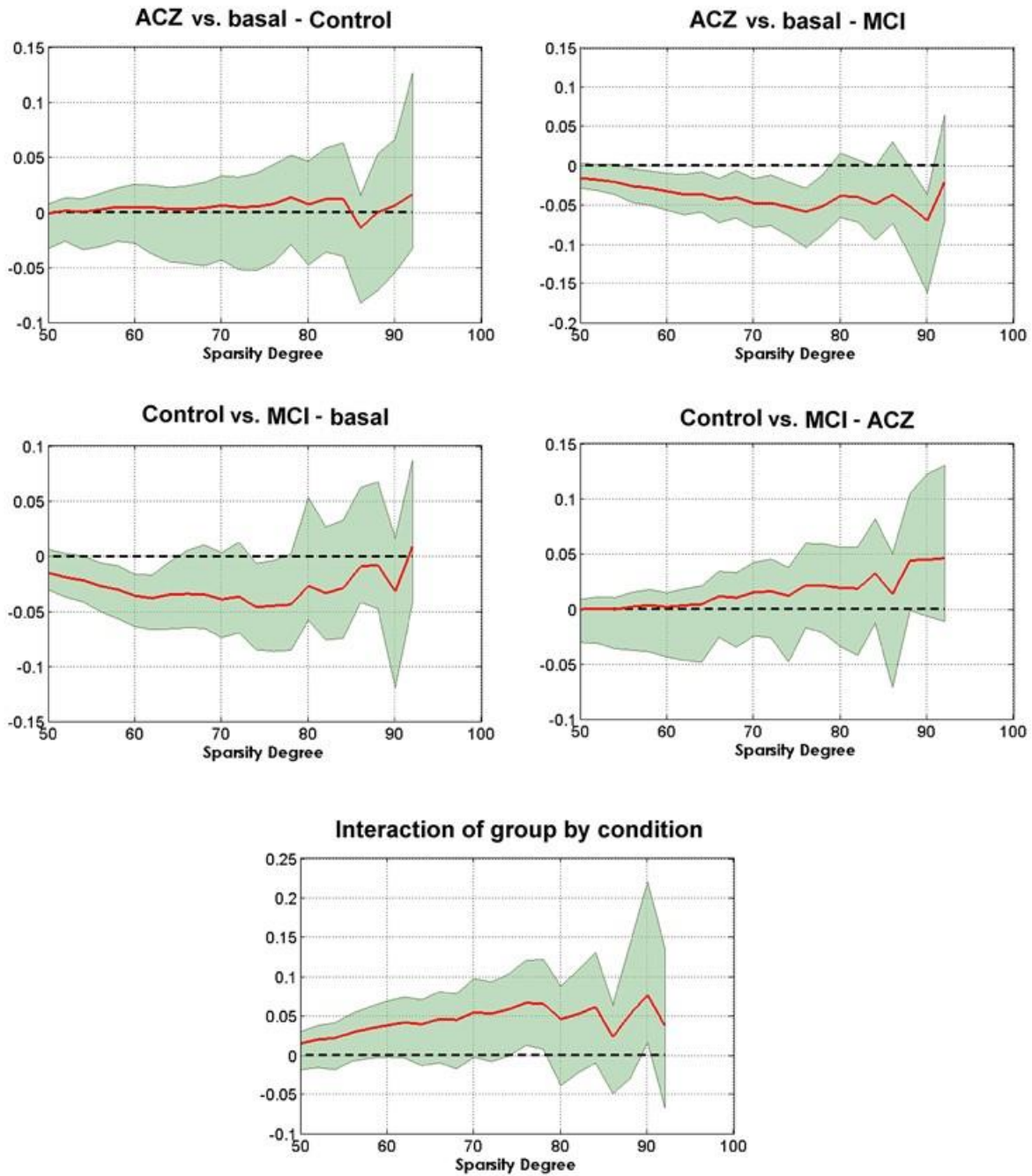
Group	p-value	Extent (voxels)	Brain regions
Control			
	0.002	1457	Right frontal lobe: precentral, superior (medial, dorsolateral and orbital), middle (including orbital) and inferior (opercular and triangular) gyri; rolandic operculum. Right postcentral and supplementary motor area.
	0.012	1028	Left frontal lobe: precentral, superior (medial and dorsolateral) and middle (including orbital) gyri. Left supplementary motor area
MCI			
	10 ⁻³	2470	Right frontal lobe: precentral, superior (medial and dorsolateral), middle and inferior (triangular) gyri; and supplementary motor area. Right postcentral gyrus. Right insula.
	0.012	1027	Left frontal lobe: precentral, superior (medial and dorsolateral) and middle gyri; and supplementary motor area.

p-value corrected for multiple comparisons (FWE) at cluster level.

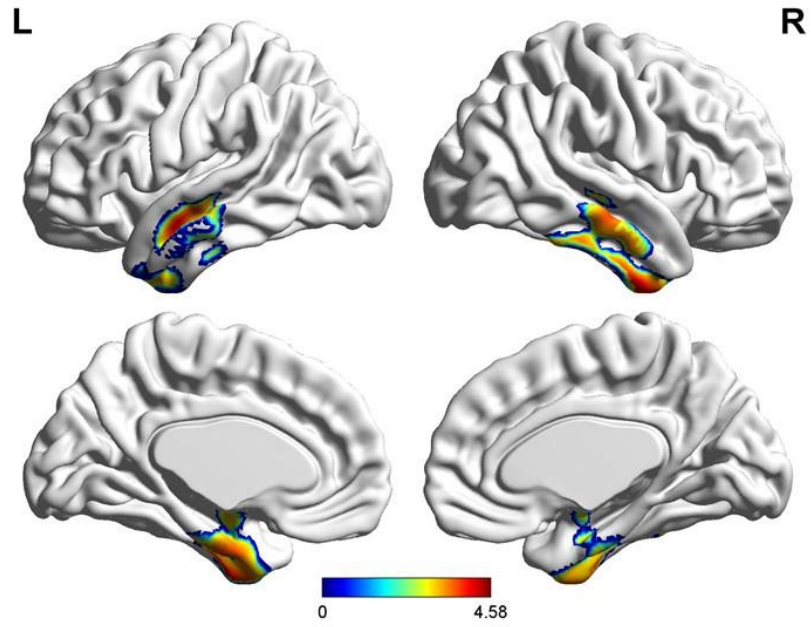
Supplementary Table S3. Brain regions with significant CBF decrease in the MCI group as compared to the control group at baseline and ACZ conditions.

Condition	p-value	Extent (voxels)	Brain regions
Basal			
	0.01	3435	Right temporoparietal cortices. Bilateral precuneus and posterior cingulate. Adjacent part of right occipital lobe and lateral temporal cortex.
	0.015	851	Left temporoparietal cortices. Adjacent parts of left occipital and temporal cortex. Left insula.
ACZ			
	0.013	1022	Bilateral precuneus and posterior cingulate. Left temporoparietal cortices.

p-value corrected for multiple comparisons (FWE) at cluster level.



Supplementary Figure S2. Differences in the global clustering coefficient (C_{global}) across the range of sparsity degree. In red, the differences, the dashed line indicates the null hypothesis and the limits of the shaded area in green indicate the 95 percent BCa (bias-corrected) bootstrap confidence interval.



Supplementary Figure S3. Brain regions with a significant grey matter volume decrease in the MCI group as compared to the control group (see also Supplementary Table S4).

Supplementary Table S4. Brain regions with a significant gray matter volume decrease in the MCI group as compared to the control group.

p-value	Extent (voxels)	Brain regions
0.02	1265	Left medial temporal lobe (hippocampus, parahippocampal and amygdala).
0.04	1026	Left lateral temporal lobe (superior, middle and inferior gyri) and fusiform gyrus. Left temporal pole.
0.01	1659	Right medial temporal lobe (hippocampus, parahippocampal and amygdala). Right lateral temporal lobe (superior, middle and inferior gyri) and fusiform gyrus. Right temporal pole.

p-value corrected for multiple comparisons (FWE) at cluster level.

References

1. Spinnler H, Tognoni G (1987) Standardizzazione e taratura di test neuropsicologici. The Italian Journal of Neurological Sciences 8, suppl 6: pp. 1-20.
2. De Renzi E, Vignolo LA. The token test: A sensitive test to detect receptive disturbances in aphasics. Brain 1962; 85: 665-678.
3. Mondini S, Mapelli D, Vestri A. Esame neuropsicologico breve. Milan: Raffaello Cortina Editore; 2005.