ON-LINE APPENDIX

MR Morphometry

An unbiased within-subject template was created by using robust, inverse consistent registration.[1] Several processing steps, such as skull-stripping, Talairach transforms, atlas registration, and spheric surface mapping and parcellations, were then initialized with the common information from the within-subject template, significantly increasing reliability and statistical power.[2] By the same processing stream, the volume of the cerebral white matter was extracted. Whole-brain volume was obtained by BrainSegNotVent output of FreeSurfer. Volume changes are plotted with respect to the second session (dehydration) because this enforces symmetric changes of opposite signs on de- and rehydration when absolute volume changes are identical. All of these volumetric measures involve partial volume corrections and surface computations at subvoxel accuracy for each individual subject.

Longitudinal changes of cortical thickness were then assessed on a vertex-wise basis, given the point correspondence implicit in the FreeSurfer outputs. All surfaces were aligned to the target shape (from the models used in FreeSurfer) by using the within- and cross-subject reference. To measure the change in subcortical/cortical surface position, we used the difference vectors between 2 time points, as projected onto the surface normal. A linear mixed effects model (see "Statistical Analyses") analysis was then applied to the signed magnitude of the difference vectors, in which negative and positive values signify the direction of changes relative to the previous time point (ie, indicate whether shrinking or expansion on de- or rehydration was detected with respect to baseline for dehydration and dehydration for the rehydration measures). Changes of vertex position directly translate into estimates of percentage thickness change and the associated *P* values for the cortical gray matter. Local estimates of mean cortical thickness change were based on spatially smoothed (full width at half maximum = 15 mm) within-subject symmetrized percentage change between successive time points,[2] spheric registration to the common target surface, intersection of cortex labels, and final averaging of the percentage change maps across subjects.

REFERENCES

1. Reuter M, Rosas HD, Fischl B. **Highly accurate inverse consistent registration: a robust approach.** *Neuroimage* 2010;53:1181–96 CrossRef Medline
2. Reuter M. Schmansky NJ, Rosas HD, et al. **Within-subject template estimation for unbiased longitudinal image analysis.** *Neuroimage* 2012;61:1402–18 CrossRef Medline

On-line Table 1: Significant post hoc tests for repeated measurements ANOVA of brain tissue water resonances[a]

Session No.		Mean Difference (Δ Signal %)	Std. Error	Sig.[b]	95% CI for Difference[c]	
					Lower Bound	Upper Bound
1 (Normohyd)	2 (Dehyd)	1.63	0.79	.03	−0.09	3.34
	3	1.61	0.89	.05	−0.33	3.56
	4	1.58	0.91	.05	−0.39	3.56
	5	1.57	0.91	.05	−0.42	3.56
	6	1.68	0.95	.05	−0.38	3.74
	8	1.63	0.93	.05	−0.39	3.65
	12	1.57	0.90	.05	−0.40	3.53
5 (Rehyd)	20	−0.37	0.17	.05	−0.75	−0.002
6 (Rehyd)	15	−0.34	0.14	.03	−0.64	−0.04
	16	−0.44	0.18	.03	−0.82	−0.06
	17	−0.39	0.16	.03	−0.74	−0.05
	19	−0.40	0.15	.02	−0.74	−0.07
	20	−0.49	0.17	.02	−0.86	−0.11
7 (Rehyd)	16	−0.31	0.13	.04	−0.61	−0.02
	19	−0.28	0.12	.04	−0.53	−0.02
	20	−0.36	0.14	.03	−0.67	−0.05
8 (Rehyd)	15	−0.29	0.12	.03	−0.55	−0.03
	16	−0.39	0.16	.03	−0.74	−0.04
	17	−0.34	0.15	.04	−0.67	−0.01
	19	−0.35	0.15	.03	−0.67	−0.03
	20	−0.44	0.18	.03	−0.83	−0.05
9 (Rehyd)	16	−0.25	0.10	.02	−0.46	−0.04
11 (Rehyd)	19	−0.30	0.13	.04	−0.58	−0.02
	20	−0.39	0.15	.03	−0.71	−0.06
12 (Rehyd)	15	−0.23	0.09	.02	−0.42	−0.03
	16	−0.33	0.09	.00	−0.52	−0.13
	17	−0.28	0.12	.04	−0.55	−0.01
13 (Rehyd)	15	−0.25	0.10	.02	−0.46	−0.04
	16	−0.35	0.13	.02	−0.64	−0.06
	17	−0.30	0.11	.02	−0.55	−0.06
	19	−0.31	0.10	.01	−0.54	−0.09
	20	−0.40	0.14	.01	−0.70	−0.01
14 (Rehyd)	17	−0.15	0.07	.05	−0.29	−0.003

Note:—Std. indicates standard; Sig., significant; Normohyd, normohydration; Dehyd, dehydration; Rehyd, rehydration.

[a] Based on estimated marginal means.

[b] The mean effect is significant at the $P \leq .05$ level.

[c] Confidence interval adjustment: least significant difference.

On-line Table 2: Correlations between volume changes of brain structures and changes in brain tissue water and serum parameters

Brain Structure	*P*	Pearson *r*
Whole brain		
▶ H_2O_{brain}	.02	0.22
▶ HTC	.00	−0.31
Cerebral cortex		
▶ HTC	.02	−0.22
Cerebral white matter		
▶ H_2O_{brain}	.00	0.34
▶ HTC	.00	−0.31
Hypothalamus/thalamus		
▶ H_2O_{brain}	.05	0.18
▶ OSM_{serum}	.04	−0.18

On-line Table 3: Significant post hoc tests for repeated measures ANOVA of morphometric data[a]

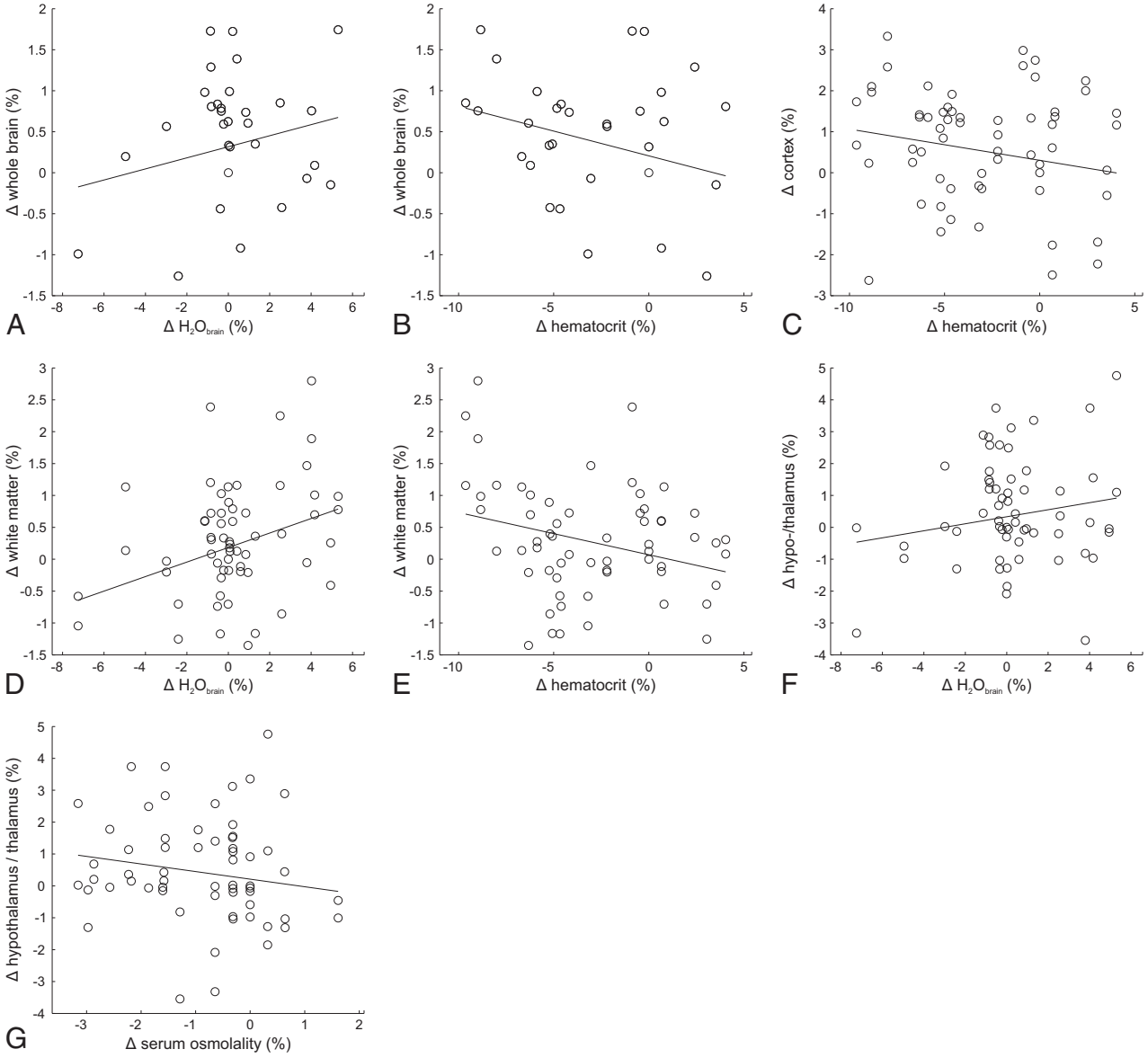
Structure	Session No.		Mean Difference (mm^3)	Std. Error	Sig.[b]	95% CI for Difference[c]	
						Lower Bound	Upper Bound
Whole brain	3 (Rehyd)	1 (Normohyd)	5897.23	2021.45	.04	278.67	11515.79
		2 (Dehyd)	10380.46	2006.96	.01	4802.17	15958.76
Cerebral cortex	3 (Rehyd)	1 (Normohyd)	3391.42	615.16	.00	2124.47	4658.38
		2 (Dehyd)	3968.89	541.42	.00	2853.80	5083.97
White matter	1 (Normohyd)	2 (Dehyd)	1261.27	368.22	.00	502.91	2019.63
Hypothalamus/thalamus	3 (Rehyd)	1 (Normohyd)	483.15	206.01	.03	58.87	907.44
		2 (Dehyd)	569.81	191.79	.00	174.82	964.80

Note:—Std. indicates standard; Sig., significant; Normohyd, normohydration; Dehyd, dehydration; Rehyd, rehydration.

[a] Based on estimated marginal means.

[b] The mean effect is significant at the $P \leq .05$ level.

[c] Confidence interval adjustment: least significant difference.



ON-LINE FIG 1. Correlation analyses of changes in serum/blood and morphometric and metabolic measures. Statistical evaluation (Pearson *r*) revealed correlations between changes of whole-brain volume and H_2O_{brain} (*A*, $r = 0.22$, $P = .02$), of whole brain volume and HCT (*B*, $r = -0.31$, $P = .00$), of cerebral cortex and HCT (*C*, $r = -0.22$, $P = .02$), of white matter and tissue fluid H_2O_{brain} (*D*, $r = 0.34$, $P = .00$), of white matter and HCT (*E*, $r = -0.31$, $P = .00$), of the hypothalamus/thalamus and H_2O_{brain} (*F*, $r = 0.18$, $P = .05$), and of the hypothalamus/thalamus and serum osmolality (*G*, $r = -0.18$, $P = .04$). FreeSurfer outputs volumes of every structure for both hemispheres separately (except for whole brain). The corresponding datasets of 15 individuals comprise 90 data points (and 45 data points for whole brain). Note that all data were normalized to values acquired during dehydration (ie, 30 data points are not visible because they collapse to zero).