Supplementary Materials

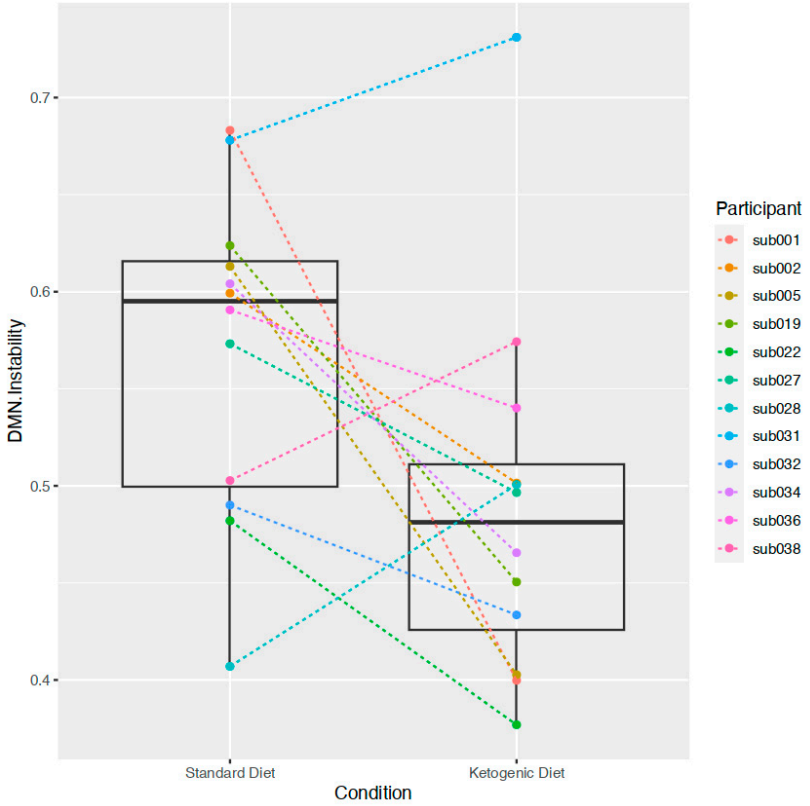
Section 1. Sample size calculation

Sample size calculation was based on findings published by Mujica-Parodi et al. [1], which presented the first evidence for stabilizing effects of ketosis on resting state functional connectivity networks. Public dataset [2] and code (https://github.com/bbantal/PAgB_network_instability) was used for calculation of network instability across a sample of 12 participants from that study. Default mode network (DMN) was chosen for calculating instabilities due to its profound energetic demand [3], extensive association with the symptomology of bipolar disorder [4], and its intrinsic predominance during the task-free resting state conditions under which our participants will be scanned. The following set of DMN instabilities was obtained for both standard diet and 1-week ketogenic diet conditions for each of the 12 participants, with τ time constant set at 1 and time windows of 24 seconds, as in the original study [1]. See Supplementary Table S1 and Figure S1:

Supplementary Table S1. Computed default mode network (DMN) instabilities by condition

Participant	DMN Instability	Condition
sub001	0.6831335	Standard Diet
sub002	0.5992506	Standard Diet
sub005	0.6130102	Standard Diet
sub019	0.6237661	Standard Diet
sub022	0.4820238	Standard Diet
sub027	0.5731876	Standard Diet
sub028	0.4069916	Standard Diet
sub031	0.6780192	Standard Diet
sub032	0.4900810	Standard Diet
sub034	0.6041005	Standard Diet
sub036	0.5906136	Standard Diet
sub038	0.5027476	Standard Diet
sub001	0.3998186	Ketogenic Diet
sub002	0.5014335	Ketogenic Diet
sub005	0.4027200	Ketogenic Diet
sub019	0.4504665	Ketogenic Diet
sub022	0.3769252	Ketogenic Diet
sub027	0.4965531	Ketogenic Diet
sub028	0.5006693	Ketogenic Diet
sub031	0.7310587	Ketogenic Diet
sub032	0.4335100	Ketogenic Diet
sub034	0.4655478	Ketogenic Diet
sub036	0.5401029	Ketogenic Diet
sub038	0.5742642	Ketogenic Diet

Supplementary Figure S1. Boxplot of participant DMN instabilities by condition



Mean difference (M_{diff}) was divided by the pooled standard deviation (S_p) of DMN instabilities between the two conditions to estimate Cohen's *d* effect size:

$$M_{diff} = M_{ket} - M_{std}$$

$$S_p = \sqrt{\frac{(S_{ket}^2 + S_{std}^2)}{2}}$$

$$d = \frac{M_{diff}}{S_p}$$

The resulting Cohen's *d* estimate was calculated to be -0.90, generally considered a strong effect. Lastly, *R* programming language package *pwr* (https://github.com/heliosdrm/pwr) was used to estimate paired samples *t*-test sample size at a significance level of 0.05, power of 0.8, and computed effect size estimate of -0.90. The resulting estimated minimal sample size was computed at 12 participants. However, this sample size is based on strict ketogenic diet intervention data, which might yield a greater effect on DMN instability than our proposed ketogenic-mimicking diet. Assuming that the effect of a ketogenic-mimicking diet is moderate as compared to the strong effect of a strict ketogenic diet, we reduced our expected effect size to -0.5, which yielded an estimated sample size of 34 participants.

References

[1] L. R. Mujica-Parodi *et al.*, "Diet modulates brain network stability, a biomarker for brain aging, in young adults," *Proc. Natl. Acad. Sci.*, vol. 117, no. 11, pp. 6170–6177, Mar. 2020, doi: 10.1073/pnas.1913042117.

[2] L. R. Mujica-Parodi *et al.*, "Protecting the Aging Brain - Diet-Study." Openneuro, 2021. doi: 10.18112/OPENNEURO.DS003437.V1.0.2.

[3] M. E. Raichle and A. Z. Snyder, "A default mode of brain function: A brief history of an evolving idea," *NeuroImage*, vol. 37, no. 4, pp. 1083–1090, Oct. 2007, doi: 10.1016/j.neuroimage.2007.02.041.

[4] B. Bi, D. Che, and Y. Bai, "Neural network of bipolar disorder: Toward integration of neuroimaging and neurocircuit-based treatment strategies," *Transl. Psychiatry*, vol. 12, no. 1, p. 143, Apr. 2022, doi: 10.1038/s41398-022-01917-x.