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MAX PLANCK INSTITUTE FOR HUMAN COGNITIVE AND BRAIN SCIENCES

Cerebellar and Cerebral Volumes Coevolve Throughout Primate Evolution

JÜLICH Forschungszentrum

HIBALL HELMHOLTZ International BigBrain Analytics & Learning Laboratory

Brain & Behaviour

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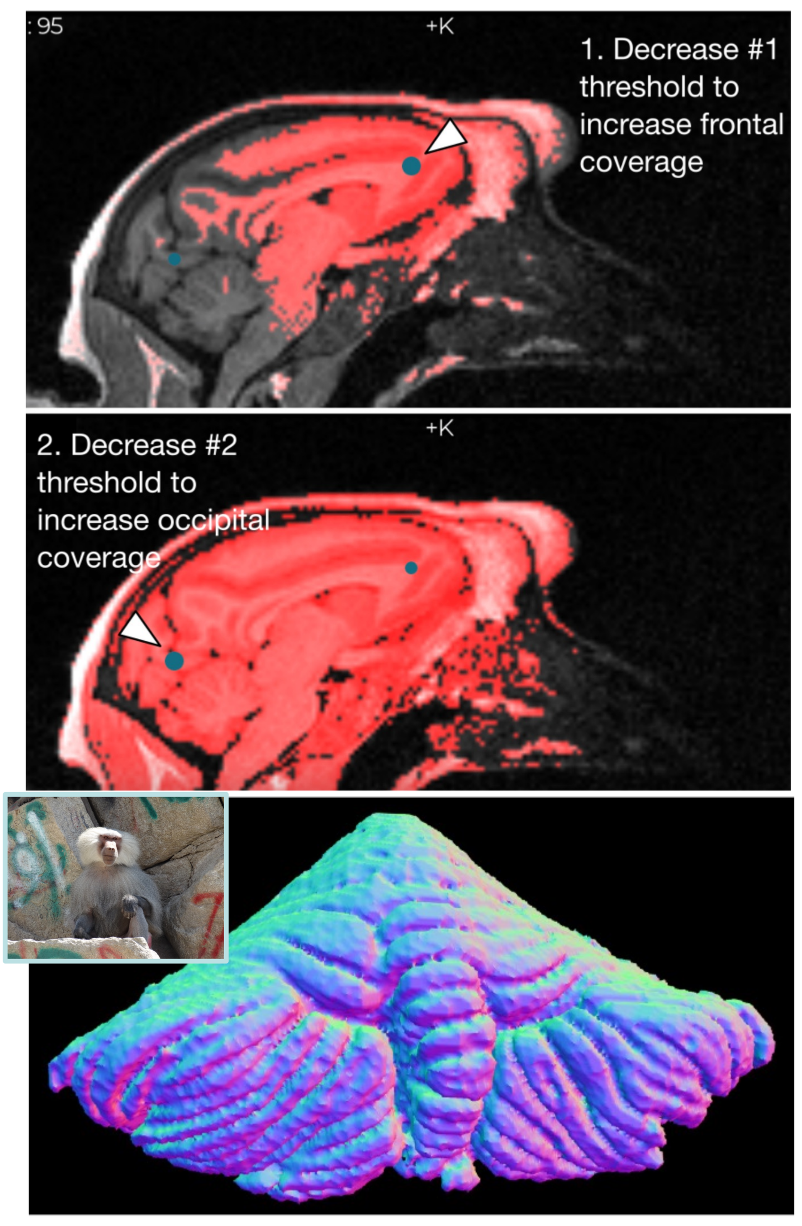
Introduction

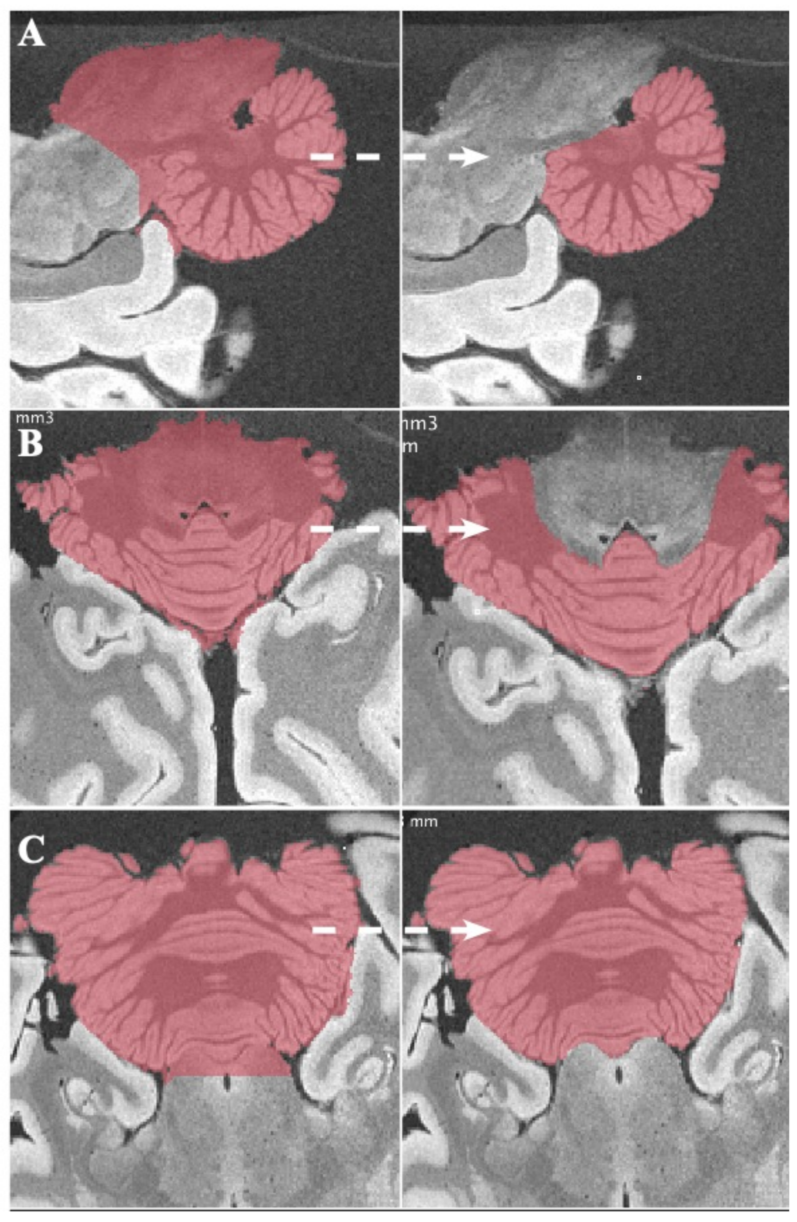
- The cerebellum is traditionally believed to be involved in motor functions only.
- However, in more recent years, a cerebellar role in higher cognitive function has been implicated.
- Through reciprocal connections with higher-order association areas of the cerebral cortex[1,2], the cerebellum is thought to support motor and non-motor functions in an analogous manner.
- Together, the cerebro-cerebellar system seems to explain primate brain size increase[3].
- In this study, by using a large phylogenetic dataset[4] (34 species, 65 specimens) **we show that the cerebellum and cerebrum scale highly predictably.**

- Our manual segmentation method is furthermore applied to Crus I-II, which we hypothesize becomes relatively larger in great apes including humans.
- We also aim to assess the influence of intraspecific variation through weighted phylogenetic regressions, and by repeating analyses with median, minimum, and maximum trait values.

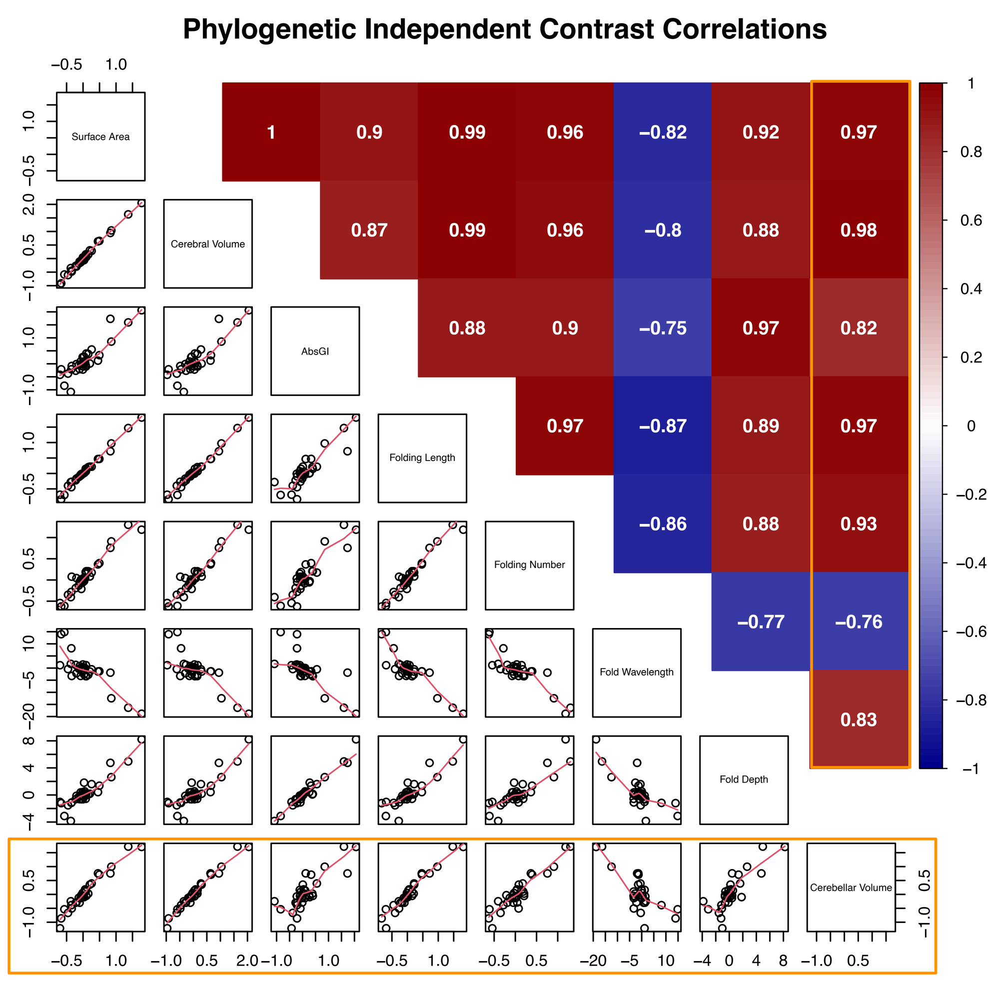
Methods[4]

- Semi-automated masks were created with the Web tool thresholdmann (https://neuroanatomy.github.io/thresholdmann).
- Manual segmentations were performed collaboratively using the Web tool BrainBox (https://brainbox.pasteur.fr)[5], which was also used to create 3D renders. The segmentations aimed to provide the most accurate cerebellar (right) and Crus I/II (not shown) segmentations.
- By employing ancestral state estimation, we were able to visualize cerebellar volumetric evolution.
- Lastly, to assess evolutionary correlation between cerebellar and cerebral volumes we used phylogenetic generalized least squares (PGLS).





Results



Cerebellar volume correlates strongly with cerebral volume and neocortical measurements

There is strong phylogenetic signal in the data, necessitating the accounting for evolutionary relationships

Inspection of the data suggests relative increases in cerebellar volume in Hominoidea and Lemuriformes

Evolutionary Model Testing

Evolutionary Model	AIC
Brownian Motion, Pagel's lambda = 1	**-1097.338**
Ornstein-Uhlenbeck, single alpha	-1089.255
Star Model, Pagel's lambda = 0	-1042.604
Early Burst	-1006.528
Ornstein-Uhlenbeck, diagonal alpha matrix	-998.4919
Ornstein-Uhlenbeck, full alpha matrix	-712.3164

PCCA

	Correlation Coefficient	Chi-square	p-value	λ (LogLikelihood)
Fixed (λ = 1)	0.95888	79.34	5.22e-19	1 (13.34)
Non-fixed (λ = variable)	0.96988	88.96	4.02e-21	**0.924 (15.41)**

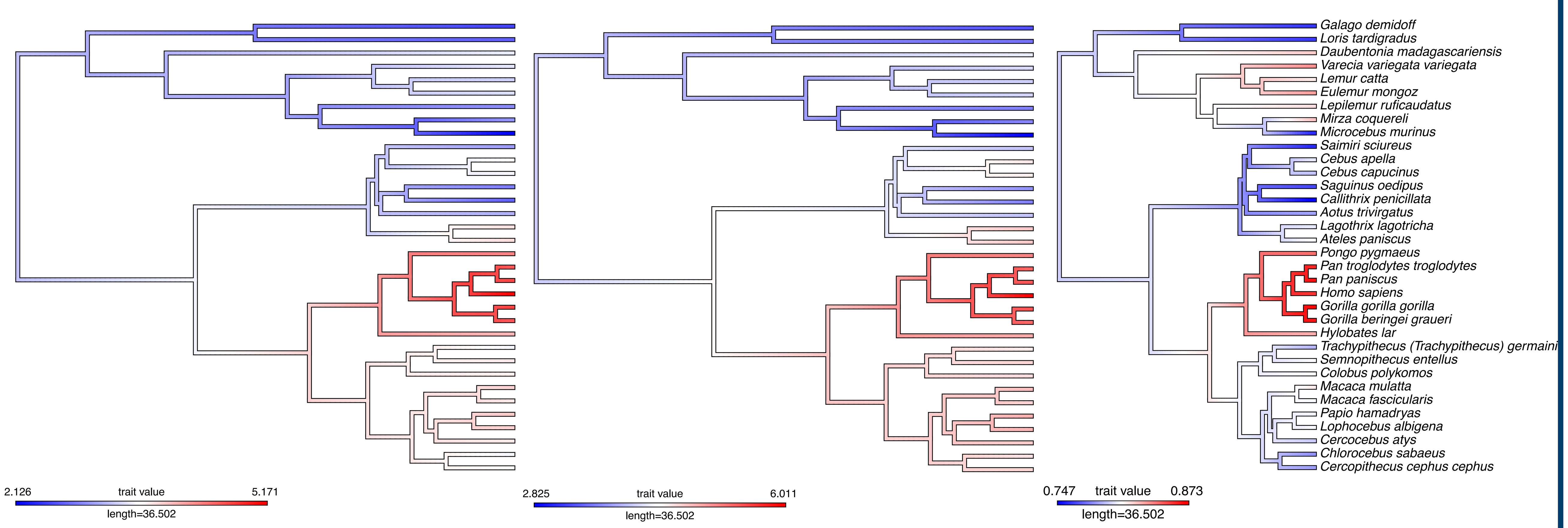
PIC Regression

	Estimate	Standard Error	t-value	Pr(>|t|)
PIC Cerebrum	**0.98700**	0.02726	36.21	<2e-16***

PGLS

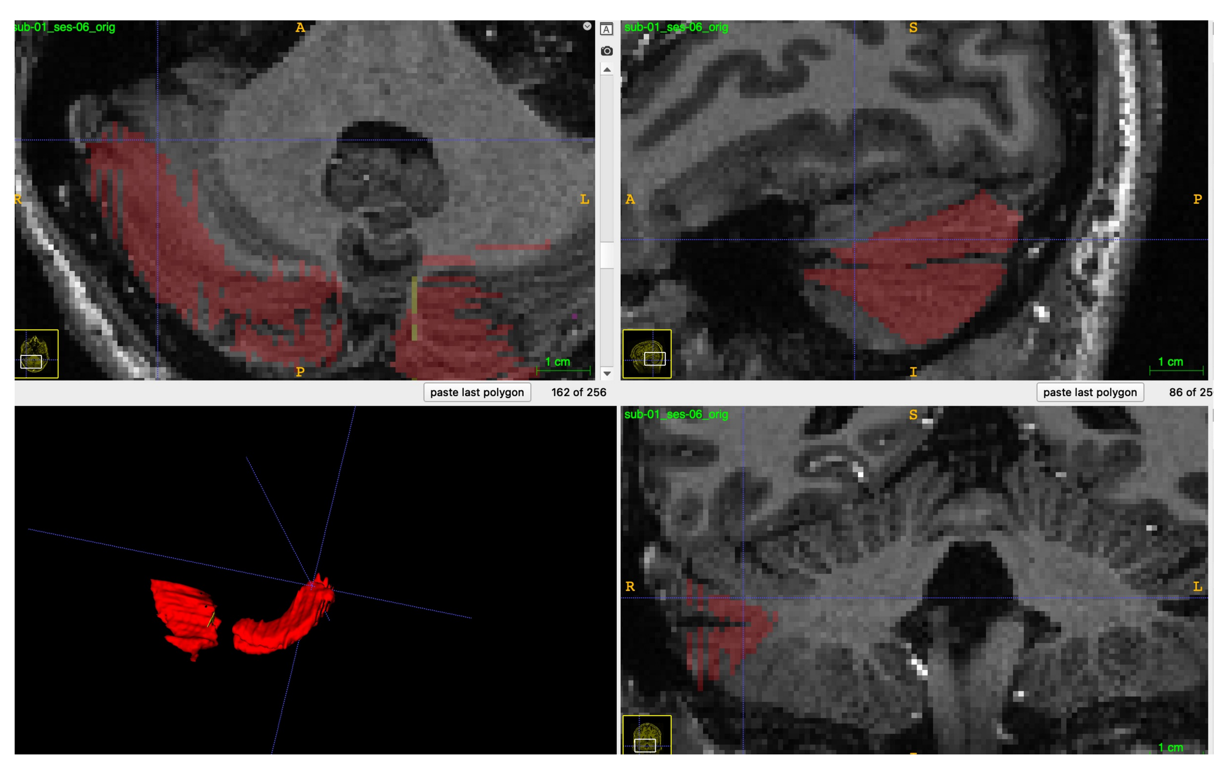
	Value	Standard Error	t-value	p-value
(Intercept)	-0.79379	0.19119	-4.15175	2e-04
Median Cerebrum	**0.98700**	0.02726	36.20824	<2e-16***

Cerebellar Volume | **Cerebral Volume** | **Ratio**



Discussion

- Our data show that the cerebellum scales highly concordantly with the cerebral cortex over primate evolution.
- Data support Brownian Motion evolution, with trait change being proportional to time since diversion.
- In Homonidea and Lemuriformes, visual inspection of the data hints at increased relative cerebellar volumes, which can be explored further by calculating branch-specific evolutionary rates[6].
- Rerunning the analyses for these groups versus other primates could reveal trends of accelerated evolutionary cerebellar growth.
- Although cerebellar and cerebral volumes strongly coevolve, we hypothesize that Crus I/II have specifically expanded within the cerebro-cerebellar system[6] (see segmentation on the right).
- Indications of such modular evolution within the cerebro-cerebellar system already exist[7]. However, in our study we incorporate ancestral relationships, as to account for statistical non-independence of our data points.
- In the future, more fine-grained (MRI or histological) comparative analyses should be undertaken in a connectivity-driven manner to deepen understanding of primate neuroevolutionary trajectories and their meaning.



References: **1.** Kelly, R. M. & Strick, P. L. Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. J. Neurosci. 23, 8432–8444 (2003). **2.** Xue, A. et al. The Detailed Organization of the Human Cerebellum Estimated by Intrinsic Functional Connectivity Within the Individual. J. Neurophysiol. 125, (2020). **3.** Smaers, J. B. & Vanier, D. R. Brain size expansion in primates and humans is explained by a selective modular expansion of the cortico-cerebellar system. Cortex 118, 292–305 (2019). **4.** Heuer, K. *et al.* Evolution of neocortical folding: A phylogenetic comparative analysis of MRI from 34 primate species. *Cortex* **118**, 275–291 (2019). **5.** Heuer, K., Ghosh, S., Robinson Sterling, A. & Toro, R. Open neuroimaging laboratory. *Research Ideas and Outcomes* **2,** (2016). **6.** Barton, R. A. & Venditti, C. Rapid evolution of the cerebellum in humans and other great apes. Curr. Biol. 24, 2440–2444 (2014). **7.** Balsters, J. H. *et al.* Evolution of the cerebellar cortex: The selective expansion of prefrontal-projecting cerebellar lobules. *Neuroimage* **49**, 2045–2052 (2010).

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