

Review of Takeshita et al. "Age, adrenal, steroids and cognitive functioning in captive chimpanzees (Pan troglodytes) for PeerJ

Basic Reporting: The basic reporting is solid. I find no important flaws.

Study Design: I believe that the study design is strong. The one clear short-coming is variation in the length of time between the blood draw and administration of the PTCB, with a much as 12 years in at least one case. This would be enough to mean that an individual cognitive data represents one age group and the hormone value a different age group. The authors are aware of this and do attempt to control for it in their original models. In addition some of the female chimps are on birth control possibly affect their DHEAS levels. However, the authors take the time to address this possibility and find no effect of birth control on DHEAS

Validity of Findings: I have no reason to doubt the findings, which are a real contribution to the literature on DHEAS among primates. They are consistent with other findings among primates including chimpanzees of age-related declines in cognition with executive function being the most noticeable.

The one point that I would like the authors to address is the possibility of a curvilinear effect of DHEAS given the age range from 11 to 52 years. Sabbi et al. 2020 report increasing urinary DHEAS levels in wild chimps until what appears to be the age of 20. The sample may be too small for a potential increase from 11 to 20 years to make a difference but I would like to see the authors at least test the possibility.

General Comments: This study considers the relationship of cognitive function, age and the adrenal steroids DHEAS and cortisol among a sample of 107 (67F:40M) captive chimpanzee ages 11-52 years. Using factor analysis of 12 items from the Primate Cognitive Battery of Cognitive, the authors derive 3 factors which they label, spatial relationships, tool use and communication and visual and sensory perception. In addition they group the chimpanzees into 4 groups based on age <25 years, 25-36 years and > 36 years based on prior classification. The authors find an interaction of age and DHEAS: cortisol ratio with spatial relationships, but none with the other groups. In addition, tool use and communication show an effect of age, while auditory and visual sensory perspective are not related to age. (I do believe that the authors mean age group rather than age.)

As the authors indicate in the discussion the divergence of the relationship of DHEAS: cortisol ratios with the three cognitive dimensions are consistent with known effects of DHEAS and cortisol on the hippocampus. So it is good to have these initial results. As the authors suggest they call for further work on the impact of DHEAS in aging.

My one criticism is that the authors might be more straightforward that the sample of chimpanzees they use are a subset of those used in Hopkins et al. 2021, and related papers. Hopkins et al. report reduction in grey matter with age. In the discussion the authors might use this fact to make a clearer connection between DHEAS: cortisol ratio and mechanisms accounting for gray matter and/or cortical thickness. Finally, the authors might want to consider the reason why DHEAS: cortisol ratio is meaningful in aging is because (at least in humans) it reflects the fact that the zona reticularis gets thinner with age while the zona fascicularis/glomerulosa does not (Parker et al. 1987).

References

Hopkins WD, Mareno MC, Neal Webb SJ, Schapiro SJ, Raghanti MA, Sherwood CC. 2021. Age-related changes in chimpanzee (*Pan troglodytes*) cognition: Cross-sectional and longitudinal analyses. *Am J Primatol.* 83(3):e23214. doi: 10.1002/ajp.23214.

Parker CR Jr, Mixon RL, Brissie RM, Grizzle WE. 1997. Aging alters zonation in the adrenal cortex of men. *J Clin Endocrinol Metab.* 82(11):3898-901. doi: 10.1210/jcem.82.11.4507.

Sabbi KH, Muller MN, Machanda ZP, Otali E, Fox SA, Wrangham RW, Emery Thompson M. 2020. Human-like adrenal development in wild chimpanzees: A longitudinal study of urinary dehydroepiandrosterone-sulfate and cortisol. *Am J Primatol.* 82(11):e23064. doi: 10.1002/ajp.23064.