Modularity and evolution of the human canine

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Background

The concepts of integration and modularity [1] provide a framework for identifying possible developmental mechanisms underlying hominin canine reduction. Previous work on non-human primates has established that the incisors comprise one module semi-independent from a premolar-molar module distally: covariation between the teeth within these modules is higher than the covariation between the modules [2]. These patterns make sense in light of the fact that tooth identity is regulated, in part, by antagonistic signaling of *Bmp4* mesially and *Fgf8* distally [3].

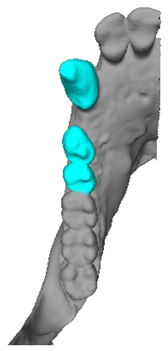
Integration and morphogenesis of the canine, and how these may have changed over human evolution, is less well known than for the rest of the dentition. Mice, model organisms in genetics, lack canines. Many studies of dental modularity have omitted the canine for logistical reasons [2,4]. Although canine size is more highly correlated with honing premolar size than with other teeth among anthropoids, it is not established if this is the case for humans [5]. Greenfield [6] suggested that canines may be influenced by incisor morphogens, citing a high prevalence of "incisor-like" canine morphologies among female anthropoids; humans were not included nor was integration specifically examined in that study.

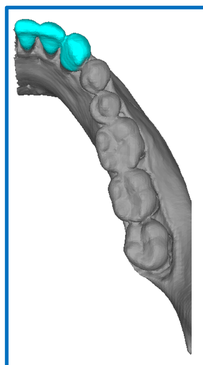
The present study bridges this previous work, testing the hypothesis that human canine reduction reflects the tooth's move from a canine-premolar honing module into a developmental module with the incisors. This hypothesis is tested by comparing patterns of tooth covariation between humans and chimpanzees. Adams' [7] Covariance Ratio measures whether hypothesized modules are tightly integrated relative to the overall covariation among teeth.

Hypotheses

H1: CP Module
Chimpanzees, but not humans, are characterized by a canine-premolar module ("CP").

Predictions
Among chimpanzees, covariance within the CP module is high relative to the overall covariance across the incisors, canine and premolars. Among humans, covariance within this module is not as exceptional.



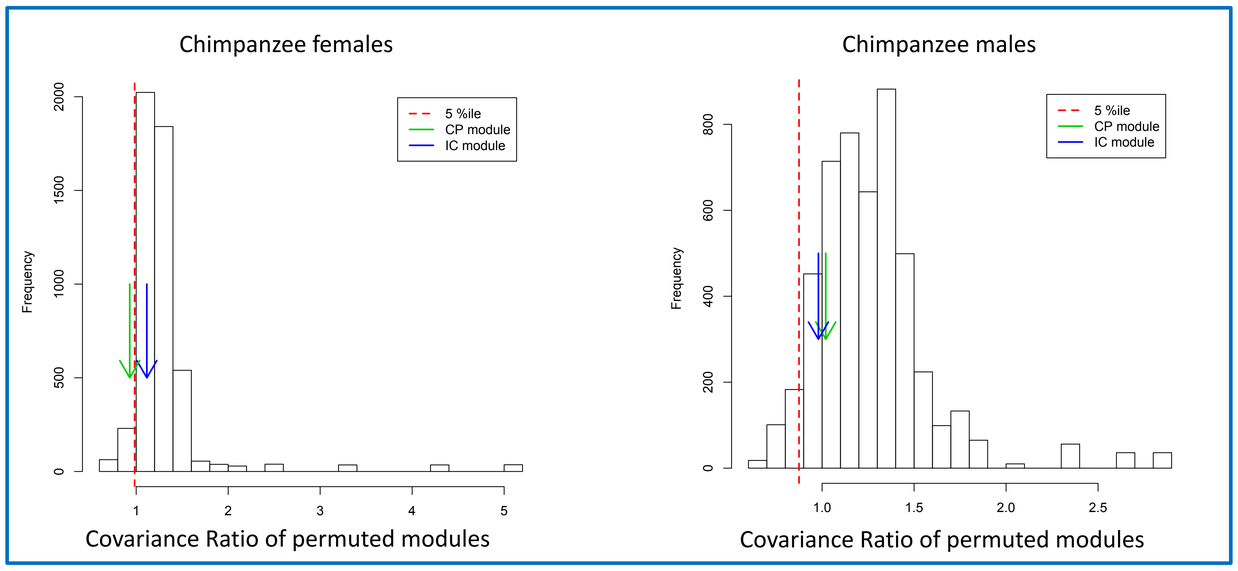


H2: IC Module
Humans, but not chimpanzees, are characterized by an incisor-canine module ("IC").

Predictions
Among humans, covariance within the IC module is high relative to the overall covariance across the incisors, canine and premolars. Among chimpanzees, covariance within this module is not as exceptional.

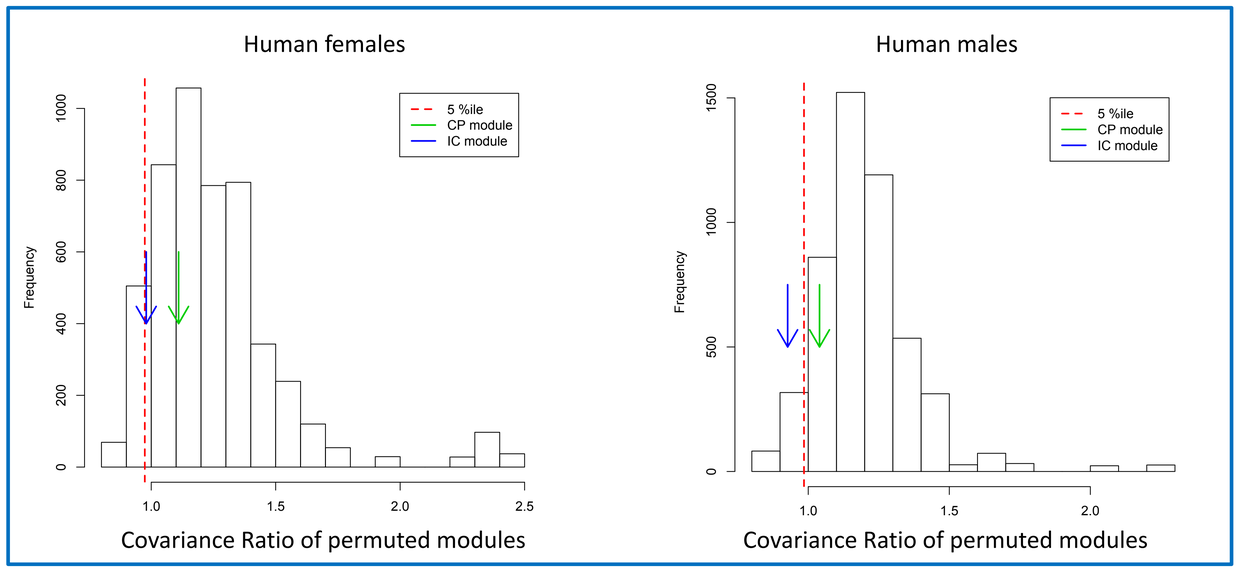
Predictions	Modularity		Integration		Covariance Ratio	
	Chimpanzee	Human	Chimpanzee	Human	Chimpanzee	Human
H1: CP module	✓	✗	↑	↓	↓	↑
H2: IC module	✗	✓	↓	↑	↑	↓

Results: Mixed support among chimpanzees



Chimpanzees	Observed CR		Resampled CR		Prediction supported?	
	CP Module	IC Module	Median	5%ile	CP Module	IC Module
Females	0.93	1.11	1.19	0.98	Yes	Yes
Males	1.02	0.98	1.24	0.87	No	No

Results: Stronger support among humans



Humans	Observed CR		Resampled CR		Prediction supported?	
	CP Module	IC Module	Median	5%ile	CP Module	IC Module
Females	1.11	0.98	1.21	0.97	Yes	Yes-ish
Males	1.04	0.92	1.16	0.96	Yes	Yes

Materials and Methods

Mandibular incisor, canine and premolar mesiodistal and buccolingual diameters were obtained from http://anthropologicaldata.free.fr/ [8]. Samples include chimpanzees (female n=59, male n=57) and Medieval Hungarians (female n=73, male n=87). Only the most complete side of the jaw was used for each individual, with antimeres included in a few cases. Outliers were identified on bivariate plots and removed. Covariance matrices were computed for each sex-specific sample in *R*, omitting missing values.

Modularity is quantified with the Covariance Ratio ("CR") [7]. CR equals one when the null hypothesis, that variables are randomly associated, is true. CR values <1 indicate covariation is greater within than between modules, while CR values >1 reflect greater covariation between modules.

To statistically assess whether the proposed modules describe covariation better than expected under the null hypothesis for each sample, permutation tests randomly assign tooth diameters to modules and recalculate the CR statistic. "Significance" of the observed CRs is indicated by the proportion of 5000 resampled CR values that are less than the observed values.

Conclusion

Results provide mixed support for the hypothesized differences in dental covariation. The observed CR values and permutation tests support the existence species-specific modules for female chimpanzees and both sexes of humans. Neither hypothesized module characterizes chimpanzee male covariation any better than a random pattern, however.

Identification of an incisor-canine module among humans suggests the canine may share a common genetic background with the incisors. *Fgf10* is expressed in the canine, premolar and molar anlagen in the short-tailed opossum [9]. If this is also true for non-human primates, the present findings suggest humans may differ in lacking *Fgf10* expression in the developing canine, but rather this anlage may be more influenced by incisor-specifying genes such as *Msx1-2* [3].

Further work is necessary to determine if the incisor-canine module identified for humans is the result of developmental interactions among these teeth, versus natural selection for a common function. The former could be tested by assessing whether tooth sizes within this module fit an inhibitory cascade pattern [11]

Acknowledgments

I would like to thank Milford Wolpoff and David Frayer for making their dental data publicly available, as well as Jean-Luc Voisin and Silvia Condemi for publishing these data online. Miriam Zelditch got me thinking about integration in grad school a million years ago, but is not responsible for any errors in the present work. Jess Beck provided comments on presentation style in the spirit of Caroline VanSickle.

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