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研究課題名（和文） 霊長類の社会進化に対する選択圧としての寄生虫の役割

研究課題名（英文） Parasites as a Selective Force in Primate Social Systems Evolution

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研究成果の概要（和文）：本研究では、霊長類の社会システムの進化において、寄生虫が選択圧になりうるかを調べた。宮崎県幸島に生息する野生ザルのメスを対象とし、実験的に寄生線虫を除去した実験群と、除去しない対照群とを比較した。その結果、まず、食物が豊富にある状況下では、実験群上位個体は、対照群個体と比べ高い体重を維持しており、寄生虫の存在がサルにエネルギー負荷を与えていることがわかった。また、実験群のメスは対照群のメスよりも高い繁殖成功率を示し、寄生虫が個体の繁殖能力を抑制しうることがわかった。これらの結果により、寄生線虫が慢性的に体内に 存在することが霊長類の個体数を調節し社会構造に影響を与えることを初めて明らかにした。

研究成果の概要（英文）：This project tested whether parasites are a selective force in primate social systems evolution. Experimental nematode parasite removal from a subset of free-ranging female Japanese macaques on Koshima, Miyazaki, showed that parasites are energetically costly; parasite removal allowed high-ranking females to maintain higher body mass than untreated females when food was abundant. More striking, treated females showed higher breeding success than control females, showing that parasites can constrain breeding potential. My previous work, and modeling done during this study, shows that social networks influence infection risk, so these results show for the first time that chronic nematode parasitism can regulate primate populations and affect social structure, making them a selective force in primate social systems evolution.

研究分野： Primatology

キーワード： Primatology　Parasitology　Coevolution　International Exchange　Social Network Analysis　Widlife Epidemiology　Disease Ecology　Behavioral Ecology

１．研究開始当初の背景

Primatologists and anthropologists have long been interested in how primate social systems evolved, particularly as a model for human social evolution. Most research on the evolution of primate sociality has focused on interactions between predation, resource availability, and conspecific factors such as infanticide [1]. These are certainly important, but they cannot account entirely for the observed diversity in primate social systems [2]. One alternative hypothesis states that infectious disease transmission also constrains host social evolution; i.e. social structure may evolve in part to reduce infection risk [3]. Evolutionary theory requires two basic assumptions of this hypothesis: (1) that infectious diseases causes variation in host fitness; and, (2) that infectious disease risk varies across hosts in relation to social variables.

The first assumption has been demonstrated repeatedly for particularly virulent viruses and bacteria [4, 5], and much less frequently for chronic infection with other parasites such as helminth and protozoan infections [reviewed in 6], with only one very recent study showing the latter to affect fitness parameters in primates [7]. However, while a number of simulation studies have also demonstrated a theoretical link between disease transmission and social structure in nature [8-10], and despite that comparative literature surveys of parasite richness across primate species add some weight to such evidence [11, 12], the empirical tests necessary to validate the theoretical relationship between disease transmission and social systems evolution are generally lacking. My own previous work with wild Japanese macaques on Yakushima showed that high-ranking and central individuals are indeed at the highest risk of infection with intestinal parasites [13, 14], adding an empirical link between infection risk and social structure and thereby setting the stage for future work to test the generality of these findings.

２．研究の目的

The aims of this research were to investigate the transmission and infection dynamics of gastrointestinal helminth parasites and test explicitly whether: (1) chronic nematode parasitism constrains host fitness; and (2) nematode parasite transmission is mediated by social networks in primate groups. The study was based primarily on a field-experimental paradigm involving parasite removal experiments, making it unique among primatological studies. Indeed, no previous study of primates had taken an experimental approach under field conditions to investigate parasite transmission; despite that manipulation of the host-parasite relationship is necessary to determine (i) causal links between host traits and infection and (ii) whether parasites do in fact alter host fitness [6]. Therefore, this project focused both on the proximate socially-mediated mechanisms of parasite reinfection following removal via anthelmintic treatment and the longer term effects of parasite removal on aspects of individual fitness (i.e. body condition and breeding success).

The Koshima population of Japanese macaques (*Macaca fuscata fuscata*), a simple and accessible model system for this research [13], offered a unique opportunity to study links between parasitism, social networks and fitness in primates – indeed, a semi-natural laboratory – because similar data cannot be obtained through observation of strictly natural populations and treatment may not be feasible or even desirable under truly natural conditions. Though I began with a focus on nematode transmission through macaque societies, the study was expanded somewhat to include theoretical work involving simulation of various directly-transmitted infectious agents. The results of the project are thus expected to be generalizable to other social animals, including humans, which at no point in their evolutionary history were free from parasitic nematodes. This work can in addition be used to inform the conservation, management and scientific communities about patterns and processes in infectious disease dynamics and their impacts on natural, socially structured host populations.

３．研究の方法

<u>3.1 Drug administration protocol</u>: Powdered medication (Drontal® Plus or Ivermectin®) was administered to 12 target female macaques at a dosage of between 0.2~0.3 mg/kg via a food substrate (peanuts or pieces of apple) 3 times per year (8 treatments in total during this study). This protocol was modified from Horii et al. [15] who performed a similar experiment with a now rarely used anthelmintic, thiabendazole.

<u>3.2 Intestinal Parasite monitoring</u>: Fresh feces (N>1800) were collected opportunistically from identified female macaques and partitions stored in 10% formalin for later parasitological analysis. Samples were also macroscopically examined for helminths. Samples were

examined via microscopy for helminth stages typically released into the environment (ova and larvae), all of which were identified and quantified in each fecal sample.

3.3 health and fitness monitoring: Each month throughout the study, body masses were recorded for each individual in the study group, including all adult female subjects. Body mass was measured by baiting each individual onto an analog balance scale using grains of wheat. Body masses provided an estimate of body condition across the study subjects. Reproductive success was measured each year during the annual birth season (June-August). Japanese macaque females may breed only once every 2-3 years at Koshima [16], so I recorded whether or not each female produced an offspring in a year in which she was eligible to do so (i.e. at least 2 years following the birth of her previous offspring). Females were then marked as successful, unsuccessful or ineligible (e.g. still lactating following a birth the previous year) breeders during each year. The success/failure ratio was determined for treated versus control females across the study (2013-2014 breeding seasons).

3.4 Behavior monitoring: Non-invasive behavioral observation was used to create interaction networks and identify behavioral changes in relation to infection and infection removal. Focal animals were selected pseudo-randomly from among the 21 adult females in the study group and followed for 15 minutes, during which their behaviors were recorded every minute, with a focus on grooming behavior to create grooming networks. Any adult female macaques within 10 meters of the focal animal were also recorded at the end of each focal sample to create proximity networks.

3.5 Social network analysis: Both directional and unidirectional, weighted social (grooming) networks were constructed using iGraph, Ucinet, SocProg and were visualized in Gephi. Individual centrality metrics such as degree, strength, betweenness and eigenvector were determined along with various global network properties such as clustering, modularity and density. These measures were used to determine the relationship between networks and infection processes, at both the individual and global network scales.

４．研究成果

Parasitological analysis of fecal samples (N=802) showed high drug efficacy against 3 of 4 nematode parasite species (nodular worm: *Oesophagostomum aculeatum*, threadworm: *Strongyloides fuelleborni* and stomach worm: *Streptopharagus pigmentatus*). The fourth species (whipworm: *Trichuris* sp.) was somewhat more resistant to treatment, though statistically significant reductions in fecal egg counts were observed for this species as well. These results show that the parasite removal protocol was effective in manipulating host-parasite dynamics, though reinfection occurred within 1-2 months post-treatment (Fig 1).

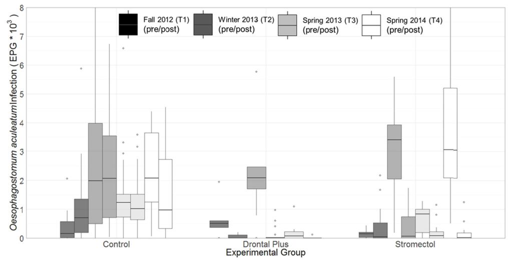

Figure 1. Fecal Egg Counts (y-axis) of exemplary nematode *Oesophagostomum aculeatum* in three experimental groups following administration of two anthelmintics (x-axis) across four treatment periods.

A general linear mixed-effects model conducted under a Bayesian statistical framework revealed a significant interactive effect between treatment, dominance rank and season (MCMCglmm, p=0.008): high-ranking females seem to receive the most benefit from parasite removal, and this is particularly true in summer and autumn when food is most abundant (Fig 2). This may suggest that treated high-ranking females benefit through increased fat storage allowed either by reduced competition with intestinal parasites for ingested calories or reduced demands for immune-mediated resistance. In addition to these body mass effects, multiple analyses (Barnard's tests and generalized linear mixed-effects models) show that reproductive success over the two breeding seasons of this study (2013-2014) was significantly higher in treated females, an effect which remained strong even after controlling for age and dominance status, whereas no a priori differences in birth rates were detected in the decade preceding this experiment. Together, these results suggest that nematode parasites are capable of regulating Japanese macaque populations via condition-dependent effects on female reproduction. This study thus provides the first empirical support for host regulation by gastrointestinal parasites in primates. Manuscripts detailing the results of this research are currently under review in the *Journal of Medical Primatology* or nearing completion.

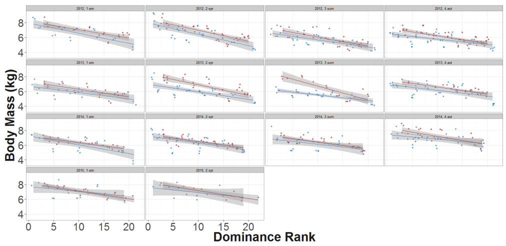

Figure 2. The relationship between dominance rank (x-axis) and body mass (y-axis) in treated (red lines) and control (blue lines) females across 14 seasons from winter 2012 to spring 2015.

While examination of fecal samples collected during this project is ongoing, preliminary results do suggest links between social network position and reinfection by intestinal helminths. However, more developed work has clearly demonstrated that theoretical and empirical links do exist between observed social networks and the spread of infectious organisms.

First, work done in collaboration with postdoctoral researcher Dr. Julie Duboscq found that individuals with large grooming networks had lower estimated lice loads in certain seasons with increased infestation (Fig 3), despite that extended networks allow for greater contact and transmission opportunities. Grooming thus effectively limits infestation and transmission of lice loads in Japanese macaques. This may not be surprising given that the original function of grooming behavior was indeed hygienic; yet, most studies of grooming in primates ignore this aspect and instead focus solely on its social function in building and maintaining relationships. This study shows that we cannot forget that grooming also has a direct impact of health through removal of external parasites and potential vectors of disease. This work is currently in review at *Scientific Reports*.

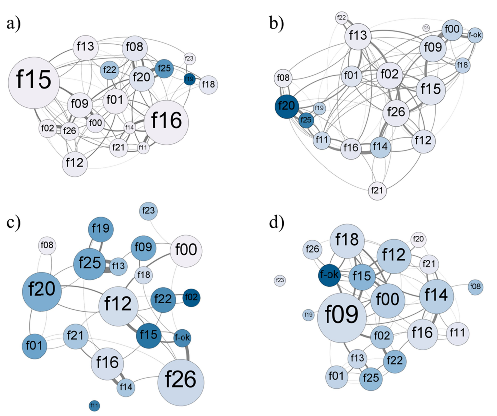

Figure 3. Seasonal grooming networks in female Koshima macaques show relationship between centrality and louse infestation. The size of each node (individual) reflects network degree centrality (number of connections) while the color reflects estimated lice loads (darker blue = higher estimate).

Second, work done in collaboration with PhD student Ms. Valeria Romano used simulations based on observed contact networks to show that pathogen spread is significantly enhanced in Japanese macaque groups on both Koshima and Yakushima (using previously collected data) when compared to randomly generated networks with the same basic properties. Interestingly, pathogen spread is likely to be more extensive and quicker within the group on Koshima (Fig 4) than the group on Yakushima, despite that the global network properties of these groups did not differ significantly. These results suggest the importance of addressing the interactive roles of both individual network positions and global network properties in predicting disease dynamics. This work is currently in review at *Animal Behavior*.

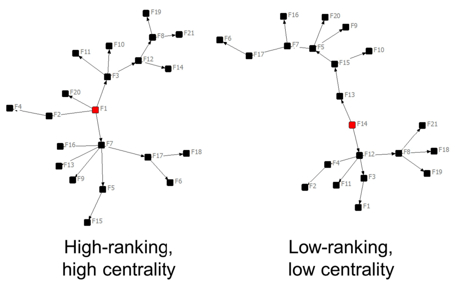

Figure 4. Transmission trees showing increased transmission efficiency when central (left) versus peripheral (right) individuals are seeded (red nodes) with a theoretical infectious agent.

In conclusion, this study showed for the first time that nematode parasites can constrain fitness parameters in a free-ranging primate population. Experimental parasite removal thus proved a key method allowing for robust interpretation of the results. Parallel work investigating transmission of gastrointestinal helminths, lice and a theoretical infectious agent further show links between social structure and the spread of infectious organisms. Collectively, these key results suggest that parasites do indeed pose a selective pressure in primate social systems evolution.

This Kakenhi project also supported work that is beginning to scale up from social networks to community networks of primates and parasites in Malyasian Borneo. This much larger and more complex project is still in the early stages of its development, but the current project was critical in getting it off the ground. The ultimate goal will be to determine whether parasites also mediate primate community structure through direct effects on primate population dynamics but also through the indirect effects of apparent competition for enemy free space.

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〔その他〕

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http://www.cicasp.pri.kyoto-u.ac.jp/people/andrew-macintosh

http://www.cicasp.pri.kyoto-u.ac.jp/news/podcasts

６．研究組織

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