



Brain Size, Metabolism, and Social Evolution

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Questions concerning the integration and scaling relationships among size, morphology, physiology, and behavior are fundamental in evolutionary biology. The evolution of brain size and structure and their association with behavior is typically examined through analyses of encephalization, brain mosaicism, and allometries among functionally specialized brain compartments. Research across diverse clades has not clarified how brain size may evolve in response to environmental, social, and cognitive requirements. Studies of metabolic and neuroarchitectural scaling across multiple levels of organization can advance our understanding of the evolution of brain and behavior. However, the analysis of brain evolution has been limited by a lack of data on brain metabolism and its relation to brain and body size, and behavior. Using ants as eusocial insect exemplars, we propose an analysis of brain evolution encompassing metabolism, brain size, and neuroarchitecture to understand how these traits scale with body size and correlate with social behavior.

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BRAIN SIZE, MOSAICISM, AND SOCIAL BEHAVIOR

Variation in brain size and structure is correlated with ecology (Liao et al., 2015; Hoops et al., 2017; DeCasien and Higham, 2019) and sociality (Kolb et al., 2013; Kotrschal et al., 2014; Dunbar and Shultz, 2017). Significant associations among brain size, structure and social behavior have been found in insects (Ott and Rogers, 2010; Eberhard and Wcislo, 2011; Muscedere and Traniello, 2012; Feinerman and Traniello, 2015; Gordon et al., 2017). Limitations of volumetric correlations have been noted (Healy and Rowe, 2007; Logan et al., 2018). Studies of the structure and number of cells, synapses, and circuits may provide important neuroethological detail (Godfrey and Gronenberg, 2019), although comparative studies of individual neurons (Giraldo et al., 2013) and synaptic processing capability (Falibene et al., 2015; Gordon and Traniello, 2018; Gordon et al., 2019; Groh and Rössler, 2020) vary in degree of linkage with behavior. Volume (or mass) data are indeed required to understand scaling of cellular metrics such as synaptic density (Yilmaz et al., 2016) or neuromodulator titer, and can provide insight into sex-specific brain differentiation (Kiesow et al., 2020) and regional investment associated with social network size (Noonan et al., 2018). Metrics of brain size and mosaicism will continue to contribute to understanding brain architecture in sociobiological contexts.

Ranging in size from microscopic wasps to goliath beetles, insects provide diverse models for studying relationships among brain size, metabolism, and behavior (Rittschof et al., 2015; Rittschof and Schirmeier, 2017). Ants exhibit robust behavioral performance at miniature size and remarkable cognition as individuals (Giurfa, 2019) and groups (Sasaki and Pratt, 2018). Colonies may be composed of polymorphic workers that divide labor according to size and/or exhibit complex collective behaviors. The impact of worker cognitive demands and colony-level capabilities on brain size and metabolism has only begun to be investigated. Variation in ant worker size—from minute *Carebara atoma* to “huge” *Dinoponera*—and colony complexity

provides outstanding opportunities to examine brain metabolism in relation to individual and group behavior.

Clade-specific brain scaling relationships, and their relation to behavior, require explanation. For example, diphasic allometry of brain mass to body mass indicates a significant increase in slope below a particular body size in some species; this may reflect limitations of investment in neural tissue in small bodies (Seid et al., 2011; van der Woude et al., 2013; Grootjans and Schmid, 2017; Polilov and Makarova, 2017). Fungus-growing ants, whose workers may have task specializations associated with their agrarian habits, show a reduced allometric slope of brain mass to body mass relative to other ants and a higher body mass at which diphasic allometry occurs (Seid et al., 2011). Relative antennal lobe volume is positively correlated with colony size, but decreases in species with strong worker polymorphism and task specialization (Riveros et al., 2012). In the desert ant *Cataglyphis*, species forming large colonies have workers with significantly larger brains than those with small colonies (Wehner et al., 2007). These studies suggest that brain size, body size, behavior, colony size, and social complexity are related.

METABOLIC SCALING AND BRAIN OPERATION COSTS

Metabolism is considered highly significant to brain evolution because brains are energetically expensive (Aiello and Wheeler, 1995; Isler and van Schaik, 2009). Larger brains may allow increased information processing; therefore, the increased cost of larger brain size implies selection for cognition in vertebrates (Pontzer et al., 2016; Dunbar and Shultz, 2017; DeCasien and Higham, 2019) and insects (Niven and Laughlin, 2008). However, there are few studies on brain metabolic scaling (West et al., 2002; Prothero, 2015) that relate brain size and metabolism. Furthermore, it is unclear whether theories of brain metabolic scaling apply to insects, whose brain structure, neuron physiology, and small size may differ in information-processing ability from vertebrates (Laughlin et al., 1998; Faisal et al., 2005; Niven and Farris, 2012; Sengupta et al., 2013). Analyses of size-related constraints on metabolism (Darveau et al., 2002; West and Brown, 2005; Fonseca-Azevedo and Herculano-Houzel, 2012), life-history traits (Harrison, 2017), and brain size evolution (Harrison et al., 2002; Isler and van Schaik, 2006, 2009; Niven and Laughlin, 2008; Navarrete et al., 2011) will benefit from the integrative study of brain size, neuron structure and brain metabolism in insects.

Brain metabolism may relate to social complexity. Kamhi et al. (2016) used cytochrome oxidase (COX) activity, a proxy for neuron metabolism (Déglise et al., 2003), to contrast brain evolution and social evolution in the weaver ant *Oecophylla smaragdina* and the garden ant *Formica subsericea*, two sister clades whose workers are equivalent in body size but differ strongly in social organization and collective intelligence. Increased social complexity in weaver ants—reflected in division of labor by worker physical castes, large colony size, and remarkable group action—was associated with larger mushroom bodies (centers of higher-order information

processing) exhibiting reduced COX activity. Increased brain size in a socially complex ant may thus be associated with reduced metabolic cost, contrasting with the assumption that increased brain size increases metabolic costs (Isler and van Schaik, 2009). Data on brain size and metabolism are therefore required to understand brain evolution.

BRAIN METABOLISM, SYNAPTIC PLASTICITY, AND DIVISION OF LABOR

Subcaste-specific metabolic scaling patterns that correlate with division of labor (Shik, 2010) and worker age can offer insight into metabolic costs of behavior and synaptic structure. Minor workers of the dimorphic ant *Pheidole dentata* show an increase in the size and number of synapses and vesicles of individual presynaptic boutons without synaptic number change in the mushroom body lip over the first 3 weeks of adult life (Seid et al., 2005) when their task diversity (Seid and Traniello, 2006) and efficiency (Muscedere et al., 2009) increase. In contrast, *Pheidole* major workers exhibit a limited behavioral repertoire even at maturity (Mertl and Traniello, 2009). In both subcastes, age is associated with increased brain volume (Muscedere and Traniello, 2012) and declines in the density of mushroom body lip microglomeruli (Gordon et al., 2018)—synaptic structures that underlie plasticity in sensory processing capability and behavior (Groh and Rössler, 2011, 2020; Groh et al., 2014; Rössler, 2019). These changes are greater in minor workers. Synaptic transmission and plasticity are metabolically costly (Attwell and Laughlin, 2001; Harris et al., 2012; Todorova and Blokland, 2017). Therefore, increased brain metabolic rate during maturity due to increased brain size may be more pronounced in minors in association with synaptic changes underpinning their greater task diversity. Additionally, brain serotonergic immunoreactivity (Seid et al., 2008) and serotonin titers (Seid and Traniello, 2005; Muscedere et al., 2012) increase with age. Brain metabolic rate may decrease in response to increased serotonin activity (New et al., 2004; Rittschof et al., 2019) and decline with age in *P. dentata*. Recording brain and mushroom body metabolism in young and old minor and major workers can provide data to enhance our understanding of how synaptic energy costs relate to variation in neuropil volume, synaptic remodeling, and behavioral pluripotency.

FUTURE RESEARCH

Technical advances have increased the accuracy and sensitivity of metabolic research. Neville et al. (2017) recorded metabolism in intact *Drosophila* larval brains similar in volume (Cardona et al., 2010) to those of minute ant brains or large mushroom bodies (Arganda et al., 2020). Pooled samples may be needed for small compartments or, for example, to measure dissociated mitochondria activity (Rittschof et al., 2019). Additional methods can be applied. Barros et al. (2018) describe the use of 2-deoxyglucose and transgenic production of fluorescent metabolites to study brain metabolite fluxes, and at the

organismal level, whole-body respirometry (Waters et al., 2017; Lighton, 2019) enables measurement of the metabolic rates of workers and colonies. Computational neuroimaging (Arganda-Carreras et al., 2017) accelerates collateral volumetric data collection for scaling studies. Proof of concept is clear, and a strong methodological foundation supports empirical studies on brain metabolism, size, and structure in ants. Variation in social complexity, worker body size, species richness, and ecology, as well as the availability of robust molecular phylogenies, allow patterns of metabolic scaling to be examined in evolutionary context.

We next identify three research areas predicated on the quantification of brain metabolism.

Metabolic Tradeoffs

The expensive tissue hypothesis predicts a tradeoff in investment in the brain and other tissues (Aiello and Wheeler, 1995) and according to selfish brain theory, the brain exhibits resilience to metabolic stress by demanding energy from other systems (Peters et al., 2013). The immune system is also considered to be energetically costly and may exhibit energetic tradeoffs with the brain (Yamagata et al., 2017). These theories overlap conceptually, but have yet to be fully integrated. Insect brains may trade the cost of neural tissue with energetically costly flight muscles (Suarez, 2000; Schippers et al., 2010) or mandibular muscles (Roces and Lighton, 1995). Diversity in diet and sociality may affect systems tradeoffs: carbohydrate diets and predation are associated with alimentary tract adaptations for food exchange and alloparenting. Diet can affect energy availability, and cognitive needs may affect brain size and metabolism. Comparative studies will offer insights into energetic constraints on brain investment relative to nutritional ecology and sociality.

Multilevel Scaling Analyses

Metabolic scaling should be considered for whole brains, functionally specialized brain compartments, workers, and colonies. Compartmental allometries can reflect variation in cognitive demands associated with division of labor (Muscedere and Traniello, 2012; Gordon et al., 2017, 2019), but the energy needs of brain compartments associated with task specialization are unknown. Hypometric metabolic scaling at the colony level has been demonstrated: workers in larger colonies with lower mass-specific metabolic rates may perform tasks that have lower costs (Shik, 2010; Fewell and Harrison, 2016; Waters et al., 2017). Data on how brain metabolism scales with colony size, combined with studies on colony size-related shifts in task

distributions, can reveal the role of behavior in colony-level metabolic scaling.

Genetic and Genomic Approaches to Metabolism

Neurons meet energy demands primarily through oxidative phosphorylation, and cytochrome oxidase (COX) has been used as a proxy for neuronal metabolism (Wong-Riley, 1989; Déglise et al., 2003). COX subunit isoforms may influence cellular metabolism (Taanman et al., 1994; Kadenbach, 2017; Chicherin et al., 2019; Reguera et al., 2020). Ants and other insects exhibit genetic diversity in COX (Liu and Beckenbach, 1992; Lunt et al., 1996) that may affect metabolic efficiency (Sabir et al., 2019).

CONCLUSION

Despite the importance of brain metabolism, the relationship between brain metabolic scaling and sociality is not well understood. Hypometric scaling of metabolism to body size and colony size in ants may be due to energy efficiency associated with social complexity. However, the impact of social complexity on worker and colony-level metabolism is unclear. Additionally, synaptic plasticity is associated with age-related changes in brain size and behavioral repertoire, but associated metabolic costs are unknown. The striking variation in body size, brain size, and individual worker and collective behavior in ants can facilitate metabolic analysis at multiple levels to test theories of brain evolution. Metabolic variation—from genes and proteins to workers and colonies—can be assessed in relation to social organization.

AUTHOR CONTRIBUTIONS

ZC and JT wrote the manuscript. JT secured funding. Both authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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