

Ants as Object of Gerontological Research

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Abstract—Social insects with identical genotype that form castes with radically different lifespans are a promising model system for studying the mechanisms underlying longevity. The main direction of progressive evolution of social insects, in particular, ants, is the development of the social way of life inextricably linked with the increase in the colony size. Only in a large colony, it is possible to have a developed polyethism, create large food reserves, and actively regulate the nest microclimate. The lifespan of ants hugely varies among genetically similar queens, workers (unproductive females), and males. The main advantage of studies on insects is the determinism of ontogenetic processes, with a single genome leading to completely different lifespans in different castes. This high degree of determinacy is precisely the reason why some researchers (incorrectly) call a colony of ants the “superorganism”, emphasizing the fact that during the development, depending on the community needs, ants can switch their ontogenetic programs, which influences their social roles, ability to learn (i.e., the brain [mushroom-like body] plasticity), and, respectively, the spectrum of tasks performed by a given individual. It has been shown that in many types of food behavior, older ants surpass young ones in both performing the tasks and transferring the experience. The balance between the need to reduce the “cost” of non-breeding individuals (short lifespan and small size of workers) and the benefit from experienced long-lived workers possessing useful skills (large size and “non-aging”) apparently determines the differences in the lifespan and aging rate of workers in different species of ants. A large spectrum of rigidly determined ontogenetic trajectories in different castes with identical genomes and the possibility of comparison between “evolutionarily advanced” and “primitive” subfamilies (e.g., Formicinae and Ponerinae) make ants an attractive object in the studies of both normal aging and effects of anti-aging drugs.

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Aging is defined functionally as the age-related reduction of cognitive, motor, and physiological functions, or demographically (mathematically) as an age-associated increase in mortality [1, 2]. It is assumed that the functional degeneration and decrease in the survival are interrelated. Evolutionary theories of aging (accumulation of mutations [3], antagonistic pleiotropy [4]) attempt to predict the regularities of aging and explain the intra- and interspecies variability of the aging rate. The disposable soma theory [5] supplements these concepts and assumes that harmful mutations influencing somatic tissue can be accumulated, if resources are given prefer-

entially to the germ line. This is especially important for studying the evolution of eusocial insects: selection of females as the embryonic line and workers as the soma [6-8]. In the case of antagonistic pleiotropy, late “harmful” manifestations of a gene with the pleiotropic effect that reflect early “useful” manifestations will be different in different taxa (because they strongly depend on the species ecology) and thus, by definition, cannot explain the same character (similar pattern, universality) of aging.

This contradiction was indicated by one of the authors of the present work (V.P.S.), who proposed the concept of organism’s programmed death (acute and chronic phenoptosis) [9, 10]. According to this concept, there is the programmed death of an organism, i.e., death

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caused by induction of the self-liquidation ontogenetic program in an individual organism (phenoptosis) [10, 11]. At present, computer models have been constructed demonstrating the evolutionary benefit of phenoptosis in some situations [12-15].

Sociality provides additional benefits for the development of longevity. In many animals, skills useful for the population and acquired during the lifetime are transmitted to young individuals by training, thereby increasing their adaptation and general resistance of the population to the environment. The longer the older generation lives, the greater training it will give to the younger individuals who also can have the "longevity gene". In social animals, there are more occasions for training than in non-social ones, in which parents can train only their own children but not adult descendants [4, 16, 17]. Social animals with intersecting young and old generations include not only mammals, but also many social insects, birds, and some other organisms. Moreover, the longevity genes can be fixed in a population due to the correlation with some adaptive trait [18].

A large gap in the current knowledge on molecular basis of aging exists because the majority of studies have been performed on short-living model organisms, such as fruit flies, nematodes, yeast, and mice [19, 20]. It had been thought earlier that the major mechanism of aging is deterioration of the repair system with age: damage gradually accumulates in all living organisms, while viability reduces. This gradual reduction of viability in many species, including insects, is described by the Gompertz equation [21].

Inconsistencies of this model have been found later. In particular, it was suggested that multi-phase survival curves persist across generations [22]. The development of bioinformatics approaches allowed to compare genes, including those responsible for aging, in different species of the same branch of the evolutionary tree [23]. Creation of full-scale gerontological databases allowed Jones et al. [8] and Magalhaes et al. [24] to perform an extensive analysis that revealed that for many species, mortality does not increase with age. Such species were formally declared non-aging, although this concept radically contradicted the adopted theory of aging as a result of accumulation of damage. In some species, death probability was found to decrease with age [25], i.e., although it seems paradoxical, it means that the repair systems should function with an increasing efficiency and the number of lesions should decrease with age.

It is known that in some groups of animals, the rate of accumulation of DNA damage and the level of reactive oxygen species generation do not correlate with the lifespan. Thus, the level of DNA damage in birds is much higher than in mammals because of a higher metabolism level; however, in some birds, aging is slower, and lifespan is greater. For instance, mute swans live longer than the great majority of mammal species [26]. Even among

mammals, there are animals that live much longer than they should, based on their size (e.g., bats [27]), although the level of damage in them is much higher than in other species because of the increased metabolism level needed for the acquired ability for flight. Naked mole rats are especially interesting, because they do not age for more than 20 years and live for more than 30 years; nevertheless, the level of lesions (including DNA damage) in them is as high as in mice and rats living for about three years [28, 29].

Baudisch and Vaupel assert that some animals live longer because they have occupied a protected ecological niche [30]. If this niche is free of danger (protected), the risk of death as a result of occasional external causes is lower. Consequently, the chance for a longer life is higher, and the selection against alleles with the late manifestation of harmful traits is stronger. However, molecular mechanisms of this process are studied insufficiently: it is not clear how exactly the ecological niche influences the aging mechanisms, why in such case the damage should accumulate more slowly, etc. The same also concerns the trade-offs [7, 31] between resources directed for the reproduction and organism maintenance, e.g., repairs that slow down aging and increase the lifespan. The mechanisms of resource redistribution are still unknown. Finally, there are some aspects that have attracted an increasing interest of researchers during the last years, such as a sharp slowing down of aging and increase in the lifespan in social animals as compared to non-social ones, which also cannot be explained by the theory of damage accumulation. It is known that in the eusocial naked mole rats, the lifespan and the resistance to accumulation of damage are greater than in non-social or non-eusocial mole rats [32].

Similar benefits of sociality (and not the influence of genetic changes) also manifest themselves in primates. Note that in humans, sociality together with the technological progress have increased so much that the average lifespan has tripled during the last 150 years [33]. The number of centenarians has grown sharply, and the probability of death in the developed countries (first of all, in Japan and Sweden) does not increase from birth until 50-60 years of age. It has been assumed that humans and naked mole rats have escaped the influence of natural selection due to a very advanced sociality, [34]. There is an alternative explanation: sociality increases the defense of an organism, decreases the probability of accidental death, and thus, strengthens the selection against harmful mutations with late effects.

The above-presented data have increased the interest to the mechanisms of aging in other eusocial animals, in particular, insects: bees, wasps, ants, and termites. The biology of aging of honey bee has been studied rather well due to the great economic importance of this species, although, certainly, not so comprehensively as the aging biology of drosophila, which is a traditional object of

study for genetics and biogerontologists. In honey bees, only the queens have a long lifespan (>8 years), whereas the workers live for 0.2-0.4 year (summer individuals) and the hibernating individuals live up to 0.9 year; therefore, it is difficult to study their aging in detail [35]. We believe that from the standpoint of gerontology, ants are the most promising social insects to study lifespan and aging, because in ants, not only queens, but also workers have sufficiently long lifespans, which makes it possible to obtain life survival data and study the influence of various biologically active substances on the lifespan.

ANTS

From the view point of ethology and ecology, ants are one of the most progressive insect families [36]. All species live in multi-year communities with the highest (eusocial) level of organization. The workers are capable of complex forms of training and solving analogs of elementary logical problems. Ants are found worldwide, except the Antarctica and some remote islands, and form 10-25% of the biomass of terrestrial animals [37]. The biology of ants is significantly different from that of short-living fruit flies with their solitary lifestyle, as well as from wasps and bumblebees, in which the time of colony life is limited by the life of reproductive individuals of one generation. In ants, as in humans, society can develop uninterruptedly, without stages of degradation. Communities of most ant species are more advanced than the communities of honey bees, whose structural organization ends at the colony level. Ants colonies often unite and form supercolony settlements containing several hundred nests [38]. However, on the evolutionary tree, ants are situated very far from humans. The societies of ants and humans may be compared with large reservations, since in humans, unlike ants, there is no division into sexual and asexual castes. Nevertheless, many aspects also have a general biological significance. Therefore, studying the life of ants has never been a narrow-specialized problem. In many aspects, the anthill is a convenient model object to study the principles of organization and development of complex social systems, population structure, and coenoses, as well as other important scientific and practical problems [39-41].

Ant colonies represent complex personalized communities with a division of labor and advanced system of communication and self-organization that allow individuals to coordinate their activities when performing the tasks that are beyond abilities of a single individual [38]. It is known that ants possess an advanced "language" and are capable of transmitting complex information to each other [42]. Moreover, ants support highly developed symbiotic relations with other insects, fungi, bacteria, and plants [43]. Recently, due to the progress in the cultivation methods, it has become possible to maintain almost

any ant species for a long time. For productive experimental work in the field of gerontology, it is first necessary to collect and analyze the data on the ant lifespan and aging, and this was the purpose of the present work.

Social insects live much longer than the solitary ones [44]. In ants, there is also a great variability in the lifespan among genetically identical queens, workers (unproductive females), and males. The queens live, on average, approximately 500 times longer than the males and 10 times longer than the workers [19]. Ant queens and workers originate from diploid eggs; their further development is only tentatively predetermined, whereas its final result depends on the needs of the colony. The final determination of the castes occurs at the early larval stage and depends on many factors, in particular, temperature, amount of food for the larvae, and the presence of the queen [45-47].

In bees, more prolonged feeding with royal jelly results in the formation in the queen of the epigenome different from the epigenome of a working individual. Such epigenetic differences induce endocrine changes that manifest themselves in the increased synthesis of the juvenile hormone and activation of the TOR (target of rapamycin) signaling pathway, as well as in the modulation of the insulin signaling pathway in the "royal" larvae. In adult individuals, these processes influence the synthesis of vitellogenin (a precursor of the egg yolk that markedly affects many aspects of insect ontogenesis) [48].

It has been shown that the action of certain food factors during the larval stage leads to a significant increase in the juvenile hormone level in the larvae of bee queens [49]. The synthesis of vitellogenin plays an important role in the development and retention of the age-associated polyethism (division of functions among the workers) in bees and ants. Thus, in *Ectatomma tuberculatum* (Ectatomminae) workers, secretion of vitellogenin changes with age: it starts approximately on the fifth day of the imago life, peak on days 20-60, and terminates on day 100. The changes in the secretion levels are associated with different activities performed by the workers [50]. It was found that the unique profile of cuticle hydrocarbons synthesized by the special glands is essential for the nestmate recognition, as well as for the ant's status in its own colony [51].

LIFESPAN OF ANTS

The data on the lifespan of ant workers and queens are scarce. Thus, *Lasius niger* and *L. alienus* are very similar in their biology (close relatives), but the maximal recorded lifespan of their queens differs three times, which is unlikely (table). All the data available so far are presented in the table.

Queens with the highest recorded lifespan belong to the genera *Lasius* and *Camponotus* (Formicinae) (28.5

Lifespan of ant queens from different species

Species	Maximal recorded lifespan, years	N/L	Reference
1	2	3	4
Subfamily Formicinae			
Tribe Lasiini			
<i>Lasius niger</i>	28.5	N	[52]
<i>Lasius flavus</i>	22.5	N	[53]
<i>Myrmecocystus mimicus</i>	11	N	[36]
<i>Lasius alienus</i>	9	N	[54]
Tribe Camponotini			
<i>Camponotus fellah</i>	26	N	[55]
<i>Camponotus perthiana</i>	23.2	N	[56]
<i>Camponotus herculeanus</i>	>10	N	[36]
<i>Camponotus lateralis</i>	8	N	[36]
<i>Camponotus consobrinus</i>	>7	N	[36]
Tribe Formicini			
<i>Formica sanguinea*</i>	20	N	[52]
<i>Formica exsecta</i>	20***	L	[57]
<i>Formica fusca</i>	16	N	[1]
<i>Formica rufibarbis</i>	14	L	[52]
<i>Formica polyctena**</i>	>5.0***	L	[58]
Subfamily Myrmicinae			
Tribe Myrmicini			
<i>Pogonomyrmex owyheei</i>	30***	L	[59]
<i>Pogonomyrmex barbatus</i>	20***	L	[60]
<i>Pogonomyrmex badius</i>	18	N	[36]
Tribe Crematogastrini			
<i>Crematogaster scutellaris</i>	20	N	[61]
<i>Harpagoxenus sublaevis</i>	>14	N, L	[62, 63]
<i>Cardiocondyla emeryi**</i>	0.5	N	[64]
Tribe Stenammini			
<i>Stenamma westwoodi</i>	18	N	[65]
Tribe Formicoxenini			
<i>Leptothorax lichtensteini</i>	17	N	[66]
<i>Leptothorax exilis</i>	>16	N	[67]
<i>Leptothorax affinis</i>	12	N	[67]
<i>Leptothorax parvulus</i>	12	N	[66]
<i>Leptothorax unifasciatus</i>	12	N	[67]
<i>Leptothorax acervorum*</i>	>11	N	[67]
<i>Leptothorax rabal</i>	>10	N	[67]
Tribe Attini			
<i>Atta sexdens</i>	15.3	N	[68]
<i>Atta cephalotes</i>	13	N	[67]
<i>Sericomyrmex urichi</i>	11	N	[69]
<i>Wasmannia auropunctata**</i>	1.1	N	[70]
Tribe Pheidolini			
<i>Aphaenogaster rudis</i>	13.1	N	[71]
<i>Messor semirufus</i>	9	N	[72]
Tribe Solenopsidini			
<i>Solenopsis invicta*</i>	>7***	N	[73]
<i>Monomorium pharaonis**</i>	0.7	N	[74]

Table (Contd.)

1	2	3	4
Subfamily Ponerinae			
Tribe Ectatommini			
<i>Ectatomma ruidum</i>	8.8	N	[75]
Tribe Odontomachini			
<i>Odontomachus haematoda</i>	4.5	N	[75]
<i>Odontomachus insularis</i>	4.5	N	[75]
Tribe Ponerini			
<i>Platythyrea punctata</i>	>4	H	[76]
<i>Diacamma cf. rugosum</i>	1.9	N	[77]
Subfamily Myrmeciinae			
Tribe Myrmeciini			
<i>Myrmecia gulosa</i>	12.8	N	[75]
<i>Myrmecia vindex</i>	10.8	N	[75]
<i>Myrmecia nigriceps</i>	7.2	N	[75]
<i>Myrmecia lobicornis</i> *	2***	L	[78]
<i>Myrmecia limanica</i> *	1.8	L	[79]
<i>Myrmecia ruginodis</i> *	1.5	N	[78]
Subfamily Ectatomminae			
Tribe Ectatommini			
<i>Rhytidoponera purpurea</i>	12.5	N	[75]
Subfamily Pseudomyrmecinae			
Tribe Pseudomyrmecini			
<i>Tetraoponera anthracina</i> **	>3.1	N	[80]
Subfamily Dolichoderinae			
Tribe Leptomyrmecini			
<i>Linepithema humile</i> **	>0.9***	N*	[81]
Tribe Tapinomini			
<i>Tapinoma sessile</i> **	0.75	N	[82]

Notes: The lifespans (maximal reliably recorded data) are taken from the gerontology databases and reference books, as well as reviews [1, 44, 67].

Regardless of the source, the table presents the references to the original works. Within each tribe, species are presented in the descending order according to the maximal recorded lifespan. Within the subfamilies, the tribes are situated beginning from the tribe containing species with the highest lifespan. In nature, the majority of the studied species form preferentially monogynous colonies (for detail see [36, 45, 52, 57, 59-62, 66, 67, 72, 75-77, 83-91]). N, in nature; L, in captivity (laboratory).

* Both monogynous and polygynous colonies are known [52, 78, 79, 86, 92].

** Mainly polygynous [58, 64, 67, 70, 80, 81, 93, 94].

*** Lifespan data are obtained as a result of calculations based on the mortality rate.

and 26 years, respectively). The values above 30 years are the estimated ones, although the monograph by Keller [95] mentions the lifespans exceeding 40 years.

The maximal lifespans of worker ants vary a lot. For instance, *Cataglyphis* (Formicinae) workers live for 30 days, *Pogonomyrmex* – 30 days, *Pheidole dentata* – 4 to 5 months [96], and *Aphaenogaster* and *Myrmica* (all belong to Myrmicinae) live for 2 to 3 years [36]. Gamergates (worker ants able for reproduction) of *Harpegnathos saltator* (Ponerinae) live for about two years [97]. As to male ants, it is known that they die immediately after one

or several matings, depending on the reproduction strategy of the species [98]. We performed experiments on 15 males of *Formica rufa* (Formicinae) that were collected from five nests and placed into tube incubators. For control, 15 workers were taken from the anthill dome and placed one per tube. Into 5 of 15 tubes with the males, three workers were placed per tube. All males died within three weeks, while 90% workers stayed alive. It was concluded that the programmed death was likely triggered in the males, and not by mating. It seems possible that the program (acute phenoptosis) was initiated by

leaving the anthill, but this hypothesis should be studied additionally.

Eusociality-associated changes in the lifespan. We also performed a comprehensive using representatives of three ant subfamilies: the most evolutionary advanced Formicinae and Myrmicinae, (with the most complex social structure, the highest lifespan of queens, etc.) and, as the opposite to them, Ponerinae (the most primitive and lacking pronounced division into castes). Below, on mentioning one or another species, the subfamily which it belongs to will be indicated in parentheses.

Eusociality-associated changes in the lifespan of queens. There are unexpectedly few studies on the demographic mechanisms of evolution of the long-term life of social insects [99]. There are at least three sets of questions that should be answered: 1) What are the similarities and differences in the lifespans of four main groups of social insects: bees, wasps, ants, and termites? 2) What is the evolutionary relation between longevity and social life of insects? 3) Do biodemographic principles really exist that can be revealed by studies of lifespan in social insects [99].

Many gerontologists consider the evolution theories as a basis for understanding the causes of aging. The best-known oppositionist is Le Bourg [100] who has suggested alternative mechanistic hypotheses of aging, without any correlation between the levels of death by external causes and lifespan (which is considered in the evolutionary theories of aging). The most serious shortcoming in the picture of the world proposed by Le Bourg is the assumption that selection acts to the benefit of colonies and that this benefit is inherited from generation to generation (similarly to the theories of Lamarck) [101]. For instance, he believes that queens must have a long life, because their short lifespan would lead to the species extinction, which is not the case. The queens from polygynous (with many queens) colonies live longer than the queens from monogynous (with one queen) colonies, because in the polygynous colonies, the death of a queen is not so critical for the colony as in the monogynous colonies. This example shows that the evolutionary theories of aging should be criticized “with caution”.

Critical assessment of the concept of “trade-offs”. One of the central principles in the evolutionary theory of Kirkwood [5] claims that organisms cannot concurrently maximize all components of adaptation. Reproduction is always costly, especially for females. This leads to a fundamental trade-off between the reproduction and lifespan that is known for many animals [31]. In the majority of animals, there is an inverse correlation between the lifespan and contribution to the reproduction, i.e., the more intensively an organism multiplies, the shorter its lifespan is. Nomosocial (eusocial with multiyear nests) insects [38] are characterized by an extremely long lifespan of reproductive queens as compared to the unproductive females [7]. Thus, bee queens lay up to 2000 eggs per day for several years; nevertheless, they live at least 20 times

longer than their unproductive sisters [35]. It has been shown earlier [19, 76, 102] that their reproductivity positively influences the lifespan. The number of queens per colony is fundamentally important for the life cycle of social insects. Polygyny with colony establishment through budding has repeatedly evolved from a hereditary single queen (monogyny) and independent establishment of the colony by single queens in wasps, bees, and ants. On the contrary, the return to monogyny seems to be rare, because polygynous queens lose adaptations that are necessary for reproduction and independent establishment of colonies [102].

Moreover, the life of queens in monogynous species is significantly longer than that of queens in polygynous taxa, which indicates that the queens' lifespan is a variable feature (see [102] and table). It has been also shown that in the same socially plastic species characterized by similar levels of extrinsic mortality of queens, queens from the colonies with one or two females have significantly longer lifespans and higher fertility than queens from associations including eight queens. Since these queens do not differ in their morphology or the way of colony establishment, this study reveals that the social environment itself has a strong influence on the aging rate [103].

Eusociality-associated changes in the lifespan of workers. Kohlmeier et al. used a large sample (29 colonies of *Temnothorax longisoinosus* (Myrmicinae)) to study the relationship between the lifespan of workers, their behavioral caste, and the presence of queens in the nest [104]. If the queen dies, an intensive development of ovaries begins in all workers. During this time, the workers struggle for domination, and the winner lays haploid eggs from which males emerge. The workers of this ant species have the same morphology, but the authors subdivided them into three behavioral groups: foragers, nurses, and inactive workers. It is also known that in this species, there is an age-related polyethism – the workers become foragers from nurses. The authors have noted that during the observation period, the same individuals remained inactive workers, without changing the behavioral caste.

The authors showed that the survival of ants depended on their caste: nurses lived longer than foragers and inactive workers ($p < 0.0001$), whose lifespan was nearly the same. The survival of the nurses was higher than that of the foragers, as it could be expected, because the foragers are, on average, older. Unexpectedly, the lifespan of the nurses was longer than the lifespan of inactive workers. In the queen's absence, the workers (nurses and foragers) lived a little longer than in the queen's presence (survival on the 200th day was 32.7 and 28.1%, respectively; $p < 0.025$). The increased lifespan of the workers was not associated with the decrease in their activity, because the lifespan of the inactive workers was the least. The assumption that fecund workers received better care (cleaning, more food) was not confirmed. If this assump-

tion were true, the lifespan only of the dominant workers would have increased, which was not the case. In the struggle for domination in the queen's absence, the youngest workers, i.e., the nurses, usually prevailed. Their ovaries would have to develop most intensively. However, this was not observed (no correlation between the two factors – the queen's presence and belonging to the caste – was found). The authors assumed that the ovaries could develop with the same intensity in all the workers, because the dominant workers could not suppress ovary development in other individuals with the same efficiency as the queen did [104]. The authors suggest that the physiological changes increasing the lifespan are associated with fecundity.

We believe that by declaring that social insects are exception from the Williams's theory [4], Kohlmeier et al. [104] make an error. They neglect the fact that they do not compare reproductive females with unproductive ones (that would be correct for the above-presented conclusion). Instead, they compare the developed female (queen) with the underdeveloped workers (because if an egg developed under other conditions, a full-value individual would hatch from it, i.e., the queen). The degree of underdevelopment of a particular worker depends on: a) *the social structure of a species* (on the extent of species polyethism); b) *the stage of the colony development* (feeding deficit is more pronounced at the initial stages); and, possibly, c) *the social position of an individual* in the colony. The lifespan and the evolutionary contribution of workers and queens to the reproduction may be compared only using the "underdevelopment coefficient", which has to be evaluated in a separate series of studies.

We think that the increase in the lifespan is not necessarily (or exclusively) related with egg laying (reproduction) *per se*. Possibly, the reproductive system development (which is suppressed in the queen's presence) correlates with better provision of other organ systems or with triggering special processes directed at maintaining the viability, which eventually leads to the increase in the lifespan.

In the recent comparative study, Kramer et al. [105] showed that in eusocial species, the difference between the lifespans of the queen and the workers increases with the increase in the colony size, which suggests that the lifespan is likely to be a trait undergoing the evolution. The authors investigated whether the lifespan of the workers decreases with the increase in the colony population. They studied the mortality of *L. niger* (Formicinae) workers that were taken from the field colonies at different stages of colony development: in the beginning of the colony establishment, when the colony population was small, and later when it became markedly higher. In the laboratory, the workers lived in artificial cohorts. It was found that workers taken at the earlier stage were smaller and had lower mortality during the first 400 days of their lives than the workers born in the colonies at the later

stages. These results show that at the early stages, the colonies produce smaller workers with an increased probability of survival. These workers are gradually supplemented (and later also replaced) by bigger workers with a decreased survival probability that serve as a surplus working force with easily replaceable individuals. It seems that the observed differences in the lifespan depend not on the differences in the body size but, probably, on certain physiological mechanisms [105].

As in many insects [21], the mortality of the ant *L. niger* follows the Gompertz law, and the initial level of mortality in major workers is higher, whereas the aging rate (the exponent index) is lower [105].

Having in mind that evolution of ants proceeds, first of all, by the increase in the colony population [106], we come nearer to the understanding of the great difference between the lifespans of reproductive and unproductive individuals.

Eusociality is an evolutionary transition to a higher complexity. In eusocial groups, selection acts not only on individuals (although individual selection is an important selective force in many social insects), but also on whole colonies that in this case, represent reproductive units. An insect colony undergoes ontogenesis: the number of workers increases, and the colony reaches a certain size, at which reproductive individuals can be generated. In the first variant, in the majority of species, reproductive individuals establish new colonies. In the other variant, the colony size increases to form the supercolony [38]. Equating a colony of ants to an organism often leaves the arguments in a deadlock.

Analysis of age-related changes in social species is important for understanding the influence of the group living on the evolution of aging in a society [107].

The high lifespan of the queens and the division of labor in eusocial communities are well studied, but it is less clear which selective forces act on the short lifespan of the workers [108]. The difference between the lifespans of the queen and the workers is associated with the main problem of sociobiology: *how are the resources distributed* between the colony maintenance and reproduction? Resources for maintaining the colony can be invested into the quality or quantity of workers. Kramer and Schaible presented a theoretical optimization model that uses the hierarchic compromise of the intrinsic and extrinsic mortality to explain the development of different aging phenotypes for providing the safety of resources in the colony [108]. The model is based on two deductions. First, any investment that would result in more prolonged lifespan of the workers is lost, if an individual dies because of external causes during foraging. As a consequence, risky conditions facilitate evolution of workers with shorter lifespans. Second, short-living workers require less investments than the long-living workers, and this allows the colony to direct the resources to sexual reproduction for increasing the colony size [108].

The dependence of the adaptation benefits on the colony size was recently demonstrated [109].

Ants of the *Diacamma* genus are one of the most interesting objects for gerontology. In addition to queens and workers, the colonies of most *Diacamma* species also have gamergates (workers capable of sexual reproduction, functional females). Some species (for instance, *D. rugosum*) do not have females. When a gamergate dies, a young worker is fertilized and occupies its position. As a rule, the colony has only one reproductive individual. A series of experiments were performed on *Diacamma* sp. gamergates to investigate the influence of reproduction on the lifespan [110]. It was shown that when the workers start to reproduce (become gamergates), their average lifespan decreases to 74-88% of the lifespan in the absence of reproduction. The authors suggest that this indicates long-term "expenditures" for maintaining the colony. We believe that this confirms that the compromise between reproduction and colony maintenance negatively influences the lifespan in insects (as it is also observed in mammals); i.e., the Kirkwood's theory, if we use it correctly, is also true for eusocial insects. The authors [110] think that the short lifespan of the workers (unproductive females), in comparison with the long lifespan of reproductive females (queens), can be explained by the increased working load better than by the compromise between reproduction and lifespan [110].

It is commonly observed that in ants, with age, workers take on more and more complex and difficult tasks and not only perform such tasks themselves, but also teach other ants more efficiently. Thus, Franklin et al. [111] studied how *Temnothorax albipennis* (Myrmicinae) ants change their mobilization habits with experience. It was determined experimentally how much participation and effective performance of the tandem course (a form of mobilization that involves two ants, a scout and a mobilized one) depended on the age or experience of the worker ants. The experiments involved *T. albipennis* colonies that had different ratios of experienced to inexperienced workers from various age cohorts and investigated which ants participated in the tandem courses. It was found that workers from all age groups were capable of participating in the recruitment for mobilization; however, the inclination for the participation varied depending on the experience but not on age. Experienced individuals demonstrated higher probability to participate in the tandem courses both as leaders and mobilized workers than the younger inexperienced ants; old experienced ants created tandems more often than the old inexperienced ants. Young inexperienced ants dispersed faster and directed the work of the tandem less accurately than the old experienced ants. This study suggests that experience associated with responses to the threshold stimuli combined with age, but not the age itself, facilitated most efficient foraging by the tandem course [111].

The influence of various functional groups on the lifespan was studied in *Oecophylla smaragdina* (Formicinae) [112]. In this species, the division of labor takes place at the morphological level: the major workers carry out risky tasks outside of the nest, while the minor workers remain in a well-protected tree nest. Such a pronounced division of labor is associated with distinct differences in the extrinsic mortality risks. The evolutionary theory of aging predicts that workers die mainly because of accidental death by external causes, and this changes selection intensity with age. In accordance with this prediction, it was found that in the protected environment, the minor workers live much longer than the major ones. Consequently, the rate of aging seems to form under the influence of changes in the extrinsic mortality rate, independently of the size, reproductive effort, and genetic component [112], in correspondence with the ideas of Williams [4].

Moron et al. studied the expected lifespan of workers as a result of distribution of risky tasks among the workers in social insects [113]. A key prediction of this evolutionary model is that workers with shorter life expectancy should perform riskier tasks. This hypothesis was tested using laboratory colonies of *Myrmica scabrinodis* (Myrmicinae) ants. The tasks were modified so that they differed in the level of risk by manipulating distances, temperatures, and the presence of competitors on foraging patches. The life expectancies of foragers were shortened by poisoning with carbon dioxide or by injury through removal of spines from the propodeum (a part of the ant thorax with physiologically important openings of the respiratory and secretory systems). Both procedures significantly reduced the lifespan of the workers as compared to the untreated ants (control). It was shown **for the first time** that foragers with shorter life expectancy foraged under risky conditions more often than foragers in the control group. Therefore, the foraging strategy of workers under risky circumstances appears to be fine-tuned to life expectancy [113].

Using 20 ant species of the Formicinae and Myrmicinae subfamilies as examples, Giraldo and Traniello [114] analyzed a number of hypotheses concerning how selection could favor worker's extended lifespan. They showed that the presence of long-living workers could be favorable for the evolutionary success of the colony by promoting its adaptability which, in its turn, is associated with the increase in the colony size. The authors concluded that workers with longer lifespan ensure increased resource acquisition, efficient division of labor, accuracy of collective decision-making, enhanced colony defense, lower infection risk, and decreased energy costs of workforce maintenance. The hypothesis on the extremely rigid program of behavioral responses preventing their changes under the influence of the environment was not confirmed. On the contrary, the workers could be rather "plastic". The efficiency of their

labor depends on worker's physiological and behavioral development, experience, and mechanical wear, but these parameters could change during the life time. In the workers, neurons are constantly rearranged – from hatching to death, the sensory capabilities of ants change, and finally, the role of workers in the colony changes. In nature, the lifespan of a worker is, on average, one year. Under artificial conditions, when the death from external causes is mostly eliminated, the lifespan of workers significantly increases. Selection can positively influence this lifespan, if its advantages for the colony exceed the costs associated with the age-related increase in the amount of errors in the work, reduction of its efficiency, and maintenance of workers' metabolism [7, 76, 77, 115]. In facultatively polygynous females of *Cardicondyla obscurior* (Myrmicinae), fecundity positively correlates with the lifespan [103].

Brain plasticity. The existence of polyethism and division of labor in social insects allows some hypotheses on aging and behavior. The aging patterns of other taxa suggest that the behavioral parameters of workers are worsening with aging as a result of worsening of brain cognitive functions. The major question is how selection structures neuromorphological variations during the adaptive behavior formation. In social insects, brain structures are different in reproductive and unproductive castes, and the specialization by morphology, age, and ecology is associated with intra- and interspecies changes in the investments in functionally different brain regions [116].

In many cases, brain plasticity is associated with changes in the behavioral model. In social insects, such as bees, wasps, and ants, the plasticity of the brain region involved in the multisensory integration (the mushroom-like body) is related to switching between the tasks with different cognitive requirements [117]. The evolutionary success of ants and other social insects is thought to be inextricably linked to the division of labor among the workers.

The behavioral development of many adult worker ants follows the hierarchy of tasks, and this facilitates the division of labor within the colony. In *P. dentata* (Myrmicinae) ants, the number of tasks for the minor workers increases, from brood care inside the nest to the activities outside the nest, such as foraging and defense. The *Pheidole* workers are morphologically and behaviorally differentiated into the minor and major subcastes that manifest clear patterns of changes in the size of brain regions [116]. By analyzing the intra- and interspecies morphological and neuroanatomical covariations, integration and modularity in the organization of the brain and pathways of its development were studied in three ecotypical *Pheidole* species. Two trait clusters have been revealed, the first of which included processing of the olfactory and social information, whereas the other consisted of brain regions regulating unlocalized sensorimotor

functions. The dependence between the sizes of the brain regions in different subcastes corresponded to the level of behavioral differentiation between the minor and major workers [116]. Generally, brain regions were more differentiated in mature workers than in immature workers. The changes in the brain structure associated with the pronounced polyethism of *Pheidole* workers likely occur based on initially differentiated brain regions responsible for the species-dependent processes of maturation and behavioral development [116]. The authors have shown that dimorphous minor and major workers of different age from three different ecotypic *Pheidole* species have different patterns of changes in the size of the neuropil (clusters of nerve cell processes with multiple synaptic contacts). The brain subcompartments involved in the processing of sensory signals coming from the optic lobes and antennae, sensory integration, learning and memory (mushroom body-like organs), and motor functions (the central body and the subpharyngeal ganglion) have significantly different relative sizes determined by different investment into the neuropil, which possibly regulates the tasks depending on both the age and the subcaste [117]. The ratios between the size and degree of development of brain regions influence the brain architecture independently of the changes in its size as a whole. In particular, the size of the mushroom-like body changes with age, differs in different subcastes, and positively correlates with the complexity of tasks solved by the individual.

Giraldo et al. were the first who have comprehensively evaluated the performance of tasks during the whole life of a worker, as well as the accompanying neurobiological changes. Using *P. dentata* (Myrmicinae) as a model, they measured the efficiency of performing the tasks inside and outside the nest by four age groups of *P. dentata* workers: 20-22, 45-47, 95-97, and 120-122 days old [96]. The workers' survival under the laboratory conditions was 50% for 77 days and 25% for 117 days (according to Kaplan–Meier survival evaluation), whereas the maximum lifespan was 140 days. The ants have been observed from the pupal stage, thereby allowing the researchers to know accurately the age of each ant in the group. It was found that in 120-day-old workers (i.e., which have lived 86% of their lifespan in the laboratory), there was no decrease in the sensorimotor functions, which made it possible for these ants to perform such difficult tasks as brood care and foraging. There was no age-associated decline in the response to prey and light. No age-associated changes were found in the affected areas and level of apoptosis in the functionally specialized brain regions; no decrease in the synaptic density in the mushroom-like body was observed as well. Seid et al. [118] showed that the total number of synapses does not decrease with age.

Moreover, the brain levels of serotonin and dopamine (biogenic amines modulating insect behavior,

whose age-associated reduction could negatively influence behavior) were higher in the old workers. It seems that the efficiency of performing the tasks is based on maintaining the brain functions responsible for olfaction and motor coordination regardless of age, as well as on the retention of behavioral characteristics and absence of significant age-related decrease in the functions of neurons [96]. These results have confirmed the conclusions of the study on the role of brain biochemistry in the age-associated division of labor, in which the levels of serotonin, dopamine, and octopamine were measured in the brain of *P. dentata* workers of different age. The levels of serotonin and dopamine significantly correlated with the age of the workers and increased with maturation. Moreover, the serotonin/dopamine ratio was significantly higher in the oldest workers. The level of octopamine did not change with age, although the octopamine/serotonin and octopamine/dopamine ratios were significantly higher in the youngest *P. dentata* workers [119].

The bodies of serotonergic neurons in the optic lobes were shown to significantly increase with maturation of the major and minor workers. In old major workers (those functioning outside the nest, for instance, foraging), the number of serotonergic neurons was higher than in minor workers of the same age. The age-associated increase in the serotonergic immune reactivity, as well as enlargement of diffuse serotonin networks in the mushroom-like body, antennae, and the central complex were accompanied with the extension of the task repertoire. These results indicate that serotonin is associated with the visual system development required for detection of work-associated stimuli outside the nest, which is important for the development of workers' behavior [120]. These results have indicated a surprising plasticity and evolutionary flexibility of the neuroanatomy of *Pheidole* workers [117].

ANTS AND URGENT PROBLEMS OF BIOGERONTOLOGY

Social insects with identical genotypes that form castes with radically different lifespan are interesting model systems for identification of mechanisms regulating longevity. This field of investigation seems especially promising in the context of current theoretical concepts suggesting that aging is essentially determined by epigenetic regulation of ontogenesis and depends, in particular, on conditions of organism's development. As it has been mentioned already, the major trend of progressive (aromorphous) evolution of social insects, in particular, ants, is the community lifestyle development that is inextricably linked to the increase in the colony size. Only in a large colony an advanced polyethism can appear, large food stores can be created, the nest microclimate can be

actively regulated, etc. Finally, an increase in the colony population ensures the biological progress of social insects, because it promotes colony homeostasis and stability of reproduction [106]. Stable existence of a nest is directly linked to the increase in the colony population that promotes an increase in the lifespan of its workers (this is absent in bees for which the maximal colony size is smaller).

Despite the immense variety of insect species, only three orders (Hymenoptera, Coleoptera, and Isoptera) have relatively large numbers of representatives whose lifespan considerably exceeds one or two years [44].

Although ants are only one of the Hymenoptera families, the number of their species (~14,000) [121] is comparable with the number of bird and mammalian species taken together. The main advantage of research on insects is associated with the determinacy of ontogenetic processes. Moreover, different trajectories of aging which lead to completely different lifespan can be observed in insects with identical genomes. Because molecular and genetic differences ensuring certain ontogenetic trajectories are known, this model is useful for studying the mechanisms involved in aging and regulation of lifespan.

Differences in the gene expression are most pronounced between the queen and the worker castes (~2500 genes), whereas different castes of workers (nurses and foragers) differ from each other to a much lesser extent (~300 genes) [122]. As compared to workers, expression of genes involved in DNA repair and protein ubiquitination in the long-living queens is upregulated, as it has been demonstrated in *L. niger* ants [123, 124]. It is interesting that the parasitic tapeworm *Anomotaenia brevis* causes changes in the expression of >400 genes leading to the increase in the lifespan of the infected *Temnothorax nylanderii* (Myrmicinae) workers, as well as to their less active behavior because of the downregulation of genes associated with the muscle activity [124].

Ants, similarly to bees (unlike Diptera, including drosophila), possess a functional system of genome methylation ("biological clock" indicating the Horvath's methylation age (DNAm age)) [125, 126] and a full set of DNA methyltransferases (Dnmts) involved in the formation of ontogenetic trajectories [127]. Thus, the differences between the castes in DNA methylation were found in the Florida carpenter ant *Camponotus floridanus* (Formicinae) and the jumping ant *Harpegnathos saltator* (Ponerinae) [127, 128]. The genomes of *C. floridanus* and *H. saltator* contain large amounts of CpG, despite DNA methylation, which in other than Hymenoptera species, correlates with the deficiency of CpG (CpG suppression). It is interesting to note that no differences in DNA methylation between the reproductive and brood care phases were observed in the thelytokous (parthenogenetic) *Cerapachys biroi* (Dorylinae) ants, in which the castes are absent [129].

The key role in choosing the ontogenetic trajectory (and determining the lifespan) in Hymenoptera belongs to the same signaling pathways as those determining the longevity and aging in humans, i.e., insulin/insulin-like growth factor 1 (IGF-1) and TOR (target of rapamycin) signaling pathways [130-132].

Depending on the environmental conditions (upbringing, feeding, life experience, etc.), one or another ontogenetic trajectory is chosen in ants. The trajectory itself is regulated genetically. It is known that, by acting on the ontogenesis at a very early age (at the larval stage before pupation), when it is too early to speak about aging and predisposition for longevity, a functional (not helpless) individual can be directed into trajectories with principally (tenfold) different lifespans [133].

An urgent task of biogerontology is a comparative study of differences in the epigenetic regulation of gene expression and genetic mechanisms (cascades) taking place when an individual follows one or another ontogenetic trajectory leading to pronounced differences in the lifespan of genetically identical individuals. In mammals, even in such highly social mammals as humans and naked mole rats, this comparison would be very difficult, because no clearly pronounced discrete ontogenetic trajectories have been detected for these species. Nevertheless, identification of even slightly similar phenomena in human development is of great interest. Thus, Walker discovered the well-known at present phenomenon of growth arrest in humans that he called the neotenic syndrome [134, 135]. People with this syndrome develop very slowly, do not have menarche, and their lifespan is short (about 20 years) despite an extremely “young” state of cells and tissues (as in a 5-7 years old child). Such people cannot lead an independent life and need a lifelong care. The question about normal neoteny (retention of juvenile traits in sexually mature individuals) in ants remains open. On approaching this problem, it is necessary, first of all, to distinctly characterize the juvenile traits. It is possible that comparison of queens and gamergates can be of help in searching for the neotenic traits in ants.

Paying a special attention to the high degree of determinacy, some authors call (incorrectly) the ant colony a “superorganism”, emphasizing the fact that during the development, depending on the community needs, ants can switch ontogenetic programs that influence both their social roles and ability to learn (i.e., brain plasticity (the mushroom-like body)), and, respectively, the spectrum of tasks performed by a given individual. To address the objection that older ants are simply directed to perform tasks associated with an increased level of extrinsic mortality because of their reduced “cost” for the colony, it can be said that the colony that directs obviously unsuitable individuals for performing the most important functions (defense and foraging) has the risk of great losses in the viability and adaptation.

Usually, older workers do not reduce the volume of their task (i.e., “do not retire”), but, on the contrary, start to perform more time- and labor-consuming tasks associated with foraging at a greater distance. The phenomenon of increased load in old individuals (e.g., the increase in the flight radius in albatrosses) has been mentioned as an example of phenoptosis manifestation [136].

Moreover, it has been shown that in many types of food behavior (the tandem course, pheromone trace mobilization), older ants surpass the young ones not only in performing the corresponding tasks but also as leaders (i.e., in the transfer of experience). Franklin et al. [111] have presented an evidence of brain plasticity retention in older workers. The authors have shown that it is not a certain age of an individual that determines its participation in more risky tasks (associated with a higher extrinsic mortality risk), but rather a combination of age with experience that implies the retention of ability to learn and process information at a proper level.

The balance between the need to reduce the “costs” of unproductive individuals (short lifespan and smaller size of workers) and the benefits of experienced long-living workers possessing useful skills, preferentially, large size and “non-aging” (i.e., with no age-associated reduction of physical and cognitive abilities) apparently determines the differences in the lifespans of workers in various species of ants.

Based on the presented data, we can conclude that ants are a very attractive object for both studying “normal” aging and testing the effects of various anti-aging preparations. This is due, in particular, to such specific features of ants as a broad spectrum of rigidly determined ontogenetic trajectories of different castes with identical genomes, known changes in the levels of DNA methylation and expression of gerontogenes, and the possibility of comparison between “evolutionary advanced” and “primitive” ant subfamilies (for instance, Formicinae and Ponerinae) [127, 128, 137, 138].

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Conflicts of Interest

Authors declare no conflicts of interest.

Observation of Ethical Norms

All applicable international, national, and/or institutional guidelines for the care and use of animals were observed.

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