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Evolutionary Theories of Menopause

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Sammanfattning
Abstract

Menopause, the cessation of female reproduction well before death, is a puzzling phenomenon, because evolutionary theory suggests there should be no selection for survival when reproduction has ended. Nevertheless, menopause does exist in a limited number of species, and besides humans it has predominately evolved among toothed whales (Odontoceti). The aim of this thesis is to review both adaptive and non-adaptive theories. Of the latter, the most prominent proposes that menopause is a product of a physiological trade-offs between reproductive benefits early in life and negative late-life reproduction. Among the adaptive theories the grandmother hypothesis is the most acknowledged. This theory is based on inclusive fitness benefits gained from increasing the reproductive success of kin at an advanced age, when prospects of successfully raising additional offspring is reduced. Alternatively, the mother hypothesis suggests that increased investment in already produced offspring at late life explains menopause. There are support for both the care of mothers and grandmothers, but whether this is enough to compensate for repressed reproduction is debated. The reproductive conflict hypothesis provides a complementary explanation, and suggests that inter-generational conflict between either in-laws or kin selects the older female to shift investment into the younger female's offspring due to asymmetries in how older and younger females are related to one another's offspring. The evolution of menopause is a complex issue, containing many factors, kinship dynamics among the most important. Theories apply unequally to various species and populations, meaning an integrated approach is necessary for decrypting the evolution of menopause.

Nyckelord
Keyword
Menopause, Post-reproduction, The grandmother hypothesis, The reproductive conflict hypothesis, Inclusive fitness, kin selection, Odontoceti, *Orcinus orca*

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1. Abstract

Menopause, the cessation of female reproduction well before death, is a puzzling phenomenon, because evolutionary theory suggests there should be no selection for survival when reproduction has ended. Nevertheless, menopause does exist in a limited number of species, and besides humans it has predominately evolved among toothed whales (Odontoceti). The aim of this thesis is to review both adaptive and non-adaptive theories. Of the latter, the most prominent proposes that menopause is a product of a physiological trade-offs between reproductive benefits early in life and negative late-life reproduction. Among the adaptive theories the grandmother hypothesis is the most acknowledged. This theory is based on inclusive fitness benefits gained from increasing the reproductive success of kin at an advanced age, when prospects of successfully raising additional offspring is reduced. Alternatively, the mother hypothesis suggests that increased investment in already produced offspring at late life explains menopause. There are support for both the care of mothers and grandmothers, but whether this is enough to compensate for repressed reproduction is debated. The reproductive conflict hypothesis provides a complementary explanation, and suggests that inter-generational conflict between either in-laws or kin selects the older female to shift investment into the younger female's offspring due to asymmetries in how older and younger females are related to one another's offspring. The evolution of menopause is a complex issue, containing many factors, kinship dynamics among the most important. Theories apply unequally to various species and populations, meaning an integrated approach is necessary for decrypting the evolution of menopause.

2. Introduction

The menopause is the senescence of reproduction in females, the cessation of the menstrual cycle (Pavelka & Fedigan, 1991). According to classic life-history theory, menopause should not occur since there should not be any selection for survival after the end of reproduction (Cant & Johnstone, 2008; Williams, 1957). The menopause is a whole process of different stages of irregular menstruation and declining fertility. The final stage of the process being complete cessation of reproduction and the beginning of the post-reproductive lifespan (Pavelka & Fedigan, 1991). Besides humans only a few species go through the process of menopause, predominately toothed whales (Odontoceti) such as killer whales (*Orcinus orca*), short-finned pilot whales (*Globicephala macrorhynchus*) (Croft et al., 2015; Ellis et al., 2018; Foote, 2008; Marsh & Kasuya, 1986), narwhals (*Monodon monoceros*) and beluga whales (*Delphinapterus leucas*) (Ellis et al., 2018), but also the insect *Quadrartus yoshinomiyai* (Croft et al., 2015).

There seems to be a diffuse difference between the menopause and the post-reproductive lifespan. Traditionally, the period between the end of fertility and the end of life is defined as the post-reproductive lifespan (Croft et al., 2015), menopause being the final stage in the senescence of reproduction prior to the post-reproductive lifespan (Pavelka & Fedigan, 1991).

This period of ceased reproduction may seem as a frequently occurring phenomenon, even though it is not. Post-reproductive life has evolved independently several times amongst Odontoceti (Ellis et al., 2018). The puzzling thing is that menopause almost predominately seems to have evolved amongst the Odontoceti (Johnstone & Cant, 2010).Why might that be?

The theories to why menopause has evolved are numerous. There are both adaptive (Brent et al., 2015; Nattrass et al., 2019) and non-adaptive (Khan et al., 2020; Peccei, 2001b) theories explaining the evolution of menopause. The adaptive theories suggest that post-reproductive life is based on inclusive fitness (Brent et al., 2015), thus an older female recedes her own reproduction to instead increase the reproductive success of kin(Johnstone & Cant, 2010). Contrary, non-adaptive theories suggest that menopause simply is a product of physiological trade-off favouring early reproduction (Peccei, 2001b; Wood et al., 2000). This review covers the grandmother hypothesis, the mother hypothesis, the reproductive conflict hypothesis and the hypothesis of antagonistic pleiotropy and

discusses as to why these theories are strong or weak. The evolutionary basis of menopause yet lacks a distinct answer, as such an integrated approach of different theories is needed to fully understand the evolution of menopause.

The aim of this review is to evaluate the evolution of menopause by various evolutionary theories and assessing their viability. It will also, examine as to why post-reproductive life has evolved among species of Odontoceti in such a great extent. By evaluating the evolutionary theories of menopause and assessing their strengths and weaknesses, parts of the puzzle of menopause are in place. This review indicates the importance of an integrated approach in order to understand the concept of the evolution of menopause fully.

3. Menopause & post-reproductive lifespan

3.1 The process of menopause

Menopause is the final period of reproductive senescence among human females. It is the cessation of the menstrual cycle along with the ovulation, the process of declining reproduction leading to the beginning of a new period of life. Menopause is a physiological process that essentially every woman that live long enough experience and the effects are individual and may take up to 10 years. Males cannot experience the process of menopause since they lack the menstrual cycle, they do however experience reproductive senescence (Pavelka & Fedigan, 1991).

3.2 Definition

During the scientific history of menopause there have been divided opinions whether the process of menopause should be regarded as a physiological maturation phase of reproduction or a pathology. Perhaps both interpretations are true (Pavelka & Fedigan, 1991). In terms of viewing menopause as a pathology, according to Wilson (1966) the menopause has often been compared to diabetes. The reason for this comparison is due to that both these conditions arise from deficiencies which are to some degree treatable by supplying the restricted substances, oestrogen or insulin (Wilson, 1966, cited in Pavelka & Fedigan, 1991). However, increased levels of oestrogen only alleviate the effects of menopause and do not restore or maintain the ovulation or

the viability of reproduction (Pavelka & Fedigan, 1991). Thus, since it is not possible to prevent menopause it cannot be regarded as a pathology but more correctly a developmental stage within the normal range of senescence.

According to Williams (1957), menopause is a reproductive adaptation to life imprinted by senescence, pregnancy and birth risks, and the long juvenile time span of dependence. Because with increased age the hazards of childbirth increase as well as the rearing of an offspring requires time and energy an older female may not be ensured due to her old age. Instead the older female can allocate her investment to her already living offspring (Williams, 1957). Cohen (2004) instead claims that post-reproductive life is due to the high cost to increasing initial oocytes which suggest a trade-off.

Post-reproductive lifespan, in the broader sense, is expected among females of species where the care of kin predominately lies with females and the kin relies on the female for a long period of time. But also, in species where the female gives birth to one offspring at a time and have long birthing periods. The social structures of close kinship groups is decisive for the occurrence of post-reproductive females (Marsh & Kasuya, 1986).

Defining post-reproductive lifespan also entails some divided ideas. According to Ellis et al (2018) post-reproductive lifespans are defined as the common and prolonged survival after cessation of reproduction where the expectation of a female post-reproductive life is substantial. While Marsh and Kusyan (1986) defined a post-reproductive female if she can no longer conceive or go through a pregnancy successfully due to age-related changes to the reproductive system. In contrast, Williams (1957) wrote "*No one is post-reproductive until his youngest child is self-sufficient*." Whatever the individual definitions it seems as the common view of the post-reproductive lifespan is that of increased reproductive senescence compared to somatic senescence, the cessation of reproduction, ultimately leading to a post-reproductive life (Cant & Johnstone, 2008; Croft et al., 2017; Ellis et al., 2018; Hill & Hurtado, 1991, 2012; Lahdenperä et al., 2004; Nattrass et al., 2019; Pavard et al., 2008; Pavelka & Fedigan, 1991; Photopoulou et al., 2017).

3.3 Species of which have a post-reproductive lifespan

Besides humans some species of Odontoceti have post-reproductive lifespan. The Odontoceti are

diverse and differ in their social structures and reproductive strategies. This diversified pattern makes for an important understanding of the evolution of post-reproductive lifespan. The reproductive life history of female cetaceans (Cetacea) have shown that species of Odontoceti exhibit post-reproductive life, narwhal *(Monodon monoceros)*, beluga whale *(Delphinapterus leucas)*, short-finned pilot whale *(Globicephala macrorhynchus)*(Ellis et al., 2018) and killer whales (*Orcinus orca)*(Foote, 2008; Nattrass et al., 2019). Only the ancestral node of *D. leucas* and *M. Monoceros* showed significant post-reproductive lifespan of the ancestors of Odontoceti, while all of the other nodes showed lack of post-reproductive lifespan. This suggests that post-reproductive lifespan in Odontoceti has evolved independently three times. Once sometime before the separation of *D. leucas* and *M. monoceros* linages, once in the linage leading to *G. macrorhynchus*, and once in the linage leading to killer whales (*Orcinus orca)* (Ellis et al., 2018).

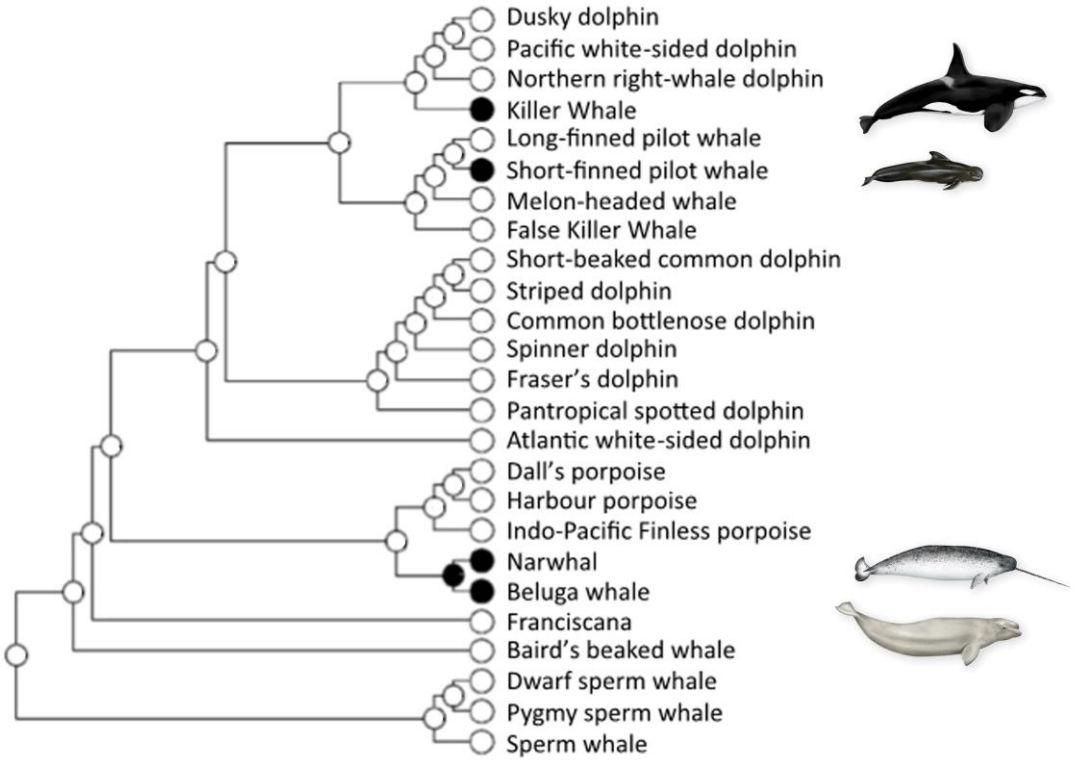

Figure 1. Phylogeny of Odontoceti that shows the evolution of post-reproductive lifespan among species. Black nodes represent post-reproduction and white nodes represent absence of post-reproduction. This phylogeny is based on Ellis et al (2018) phylogeny of post-reproductive Odontoceti.

3.4 Quantifying post-reproduction

To quantify the rate of reproductive senescence in wild populations is a difficult area of research (Ellis et al., 2018; Khan et al., 2020). According to Levitis and Lackey (2011) much of the research evaluating post-reproductive lifespan in populations is carried out by an inaccurate method of calculation. Most often post-reproductive lifespan is measured in units of time, post-reproductive time, from the cessation of reproduction to the end of life. Furthermore, they write that the contradiction of a post-reproductive lifespan is explained, broadly, by the concept that human post-reproductive lifespan is principally greater and even qualitatively different from other species post-reproductive lifespan (Levitis & Lackey, 2011).

4. The adaptive theories

4.1 The grandmother hypothesis

4.1.1 The concept

The grandmother hypothesis suggests that as females age, investing in grandoffspring increases fitness through inclusive fitness more than if they were to continue to reproduce themselves. This is because there are increased hazards with child birth with increased age and the offspring is dependent on the mother during the juvenile period and since she might not survive long enough for the offspring to survive until maturation the investment might be lost (Hawkes et al., 1998, 1998; Hill & Hurtado, 1991; Williams, 1957). The grandmother hypothesis is widely used to explain the occurrence of females living beyond their reproductive life, likely due to the fact that the theory is consistent with modern evolutionary theories as well as being logical (Hill & Hurtado, 1991). In order to grasp the concept of the grandmother hypothesis it is important to understand the costs in term of fitness. There is a constant evaluation whether the benefit of others is greater than the risk of the reproduction of oneself, and how much greater does the benefit of others need to be to outweigh the risks. This can be explained by Hamilton´s rule (Hamilton, 1964). When the fitness benefit (*B*) of investing in kin times the probability that a rare allele is shared with kin (*r*) is greater than the cost of giving up reproduction (*C*), natural selection will favour investment in kin which will evolve if it is of heritable tendency. Therefore, in terms of the grandmother hypothesis, the cessation of reproduction should evolve when:

$$\sum Br > C \qquad (1)$$

In the case of applying this equation on the grandmother hypothesis, *B* is the increasing number of kin resulting from the time a female invest in helping relatives to reproduce, *r* is the genetic coefficient of kinship of the kin helped, and *C* is the number of offspring the female could have produced if not investing time in helping kin to reproduce (Hill & Hurtado, 1991).

Evaluating the cost versus benefit side in the equation differs between situations. For example, if there is high probability for a female to die in some time lapse and her offspring is unlikely to survive if her death occurs while the offspring is juvenile, then the cost in the equation is expected to be small. This is because there is small expectancy to offspring of an older female to survive and therefore it is more beneficial to invest in kin such as grandoffspring. Another situation of evaluating the cost and benefit is that of age-specific fertility difference, that may favour reproductive senescence. For example, older females often have a low inherent fertility compared to younger females who often have a higher inherent fertility. Thus, if they both invest an equal amount in producing an offspring this would result in a low probability of a life birth for the older female while it would result in a high probability of life birth for the younger female. Therefore, the older females would gain higher fitness benefits by investing in her offspring's fertility rather than investing in her own. Thus, reproductive senescence will be favoured by natural selection whenever a females effect on kin reproductive success is greater than that of her own, also called the grandmother hypothesis (Hill & Hurtado, 1991).

4.1.2 The grandmother hypothesis applied to humans

Hill and Hurtado (1991) claim that the grandmother hypothesis is weak due to the small effect of grandmothers. This argument is based on their research on indigenous nomad hunter-gatherers of Paraguay and the evaluation of the grandmother effect amongst these individuals. They mean that because of the small grandmother effect and the fact that the potential cost outweighs the fitness benefits over the entire span of an adult female between 40 – 65 years, natural selection will not favour the senescence of reproduction. They mean that fitness benefits do rise with age but remain low due to that most females are expected to produce few offspring that will survive to adulthood and benefit from their help and also due to the weak effect of grandmothers. Not even when including the fitness benefits of females helping their younger siblings the benefits does not exceed the cost and equation 1 still does not favour reproductive senescence. Further, not even when

including helping other kin as nieces' and nephews' reproductive senescence is favoured (Hill & Hurtado, 1991).

Even though Hill and Hurtado (1991) conclude the low influence of the grandmother effect, if any, they do however mention parameters that would indeed increase the grandmother effect. Parameters such as, a significant and greater effect on the reproductive success of kin, as well as significantly greater mortality rates of births after the age of 40. If these parameters would be met in a population then natural selection would probably favour reproductive senescence. They also argue that the effect of the mother varies between populations and the condition the population is under, thereby affecting the influence of the grandmother effect. They emphasize the influence of possible confounding factors to the grandmother hypothesis, such as if there is a correlation of mother effect and father effect, if older females have offspring with reproductive success above the mean regardless of help, or if sons and daughters that reproduced without help actually received help from other kin. Also, the mother effect may not be constant when summed, where females with fewer kin may have a greater beneficial impact on their kin's reproductive success than females with more kin. All these possible confounding factors underestimate the influence of the grandmother hypothesis. Further they ask the question of why the menopause is not a facultative response. Why females with a lot of offspring cannot terminate their own reproduction to invest in already existing offspring as well as females with few offspring would continue to reproduce with increased age to produce and invest in offspring. They claim that far from every society meet the criteria to favour menopause through kin selection, yet the cessation of reproduction is universal. Therefore, the menopause must be a response to universally existing conditions. Hill and Hurtado (1991) conclude that menopause might as well be favoured through kin selection, since the grandmother hypothesis accounts for age-specific fertility decline as well as subsequent reproductive senescence. They mean that the human lifespan did not increase beyond the cessation of the female reproduction recently. By this, even though their model fails to confirm the adaptive approach, simultaneously it is not false (Hill & Hurtado, 1991).

Accordingly, Cohen (2004) agrees that the evidence for adaptive hypothesis as the grandmother hypothesis is scarce, but likewise is the evidence against adaptive hypothesis such as the grandmother hypothesis also scarce. He argues that adaptive hypothesis as the basis for post-

reproductive life is compatible but lacks causality, and that this may vary with species and populations. He also points to the importance of other hypotheses, and the difficulty in assessing their effect without sufficient data. In terms of evidence against adaptive explanation Cohen (2004) criticizes Hill and Hurtado's (1991) conclusion of the weak grandmother effect. He claims that their model lacks the ability to incorporate every relevant variable, such as the significant increase of mortality rate with age during birth (Cohen, 2004).

Among humans, there are several shortcomings of the grandmother hypothesis that also support the weakness of the hypothesis. The grandmother hypothesis can be divided into the old and the new grandmother hypothesis. The old grandmother hypothesis constitutes the benefits of early reproductive cessation to invest in offspring reproductive success, while the new grandmother hypothesis considers longevity as the result of inclusive fitness. Both the old and new grandmother hypothesis contain some shortcomings of not considered factors. Such as the lack of universal evidence for the occurrence of helping grandmothers in populations, there is also lack of sufficient support that the fitness advantages of ceased reproduction favouring increased investment in adult daughters and the grandoffspring in the mathematical model which might not be representable. There is also a problem in regard of the social structures whereas both the old and new grandmother hypothesis requires female philopatry (females stay in their natal group), which is not the universal case of social dynamics. Both these variants of the theory neglect the role of caretakers other than the mother and grandmother, which probably also is a false reflection of the reality. Besides these shortcomings mentioned the new grandmother hypothesis also possesses some further shortcomings due to the recent increase of longevity of humans, that points to longer juvenile period and longer dependence on the care of mothers. All of which points to the weak influence of grandmothers which thereby makes the grandmother hypothesis doubtable (Peccei, 2001a).

Contrary, Lahdenperä et al. (2004) mean that the grandmother effect is of substantial influence if the post-reproductive lifespan is sufficient. The length of the post-reproductive lifespan is significant for the amount grandoffspring, with increased number of grandoffspring with increased post-reproductive life. Lahdenperä et al. (2004) studied the effect of post-reproductive women for grandoffspring and thereby the inclusive fitness, they state that a post-reproductive female gains two grandoffspring for every ten years beyond the age 50 that she survives. This might be because

the longer a post-reproductive female lives after her offspring start to reproduce, the greater that offspring's lifetime reproductive success. Furthermore, they suggest that both sons and daughters benefit equally from a surving post-reproductive female (the mother), contrary to previous studies. Lahdenperä et al. (2004) mean that the fitness effects are due to the benefits of a post-reproductive female on: i) the key-life-history traits of her offspring; and ii) the survival of her grandoffspring. In addition, the grandoffspring has greater survival rates if the post-reproductive female (the grandmother) is alive during birth. Lahdenperä et al. (2004) claims that the post-reproductive life is adaptive. This might explain, at least partially, the prolonged post-reproductive life exhibited by humans (Lahdenperä et al., 2004).

4.1.3 The grandmother hypothesis applied to Orcinus orca

Grandmothers among *O. orca* of the resident ecotype has an essential beneficial influence. This species have one of the longest post-reproductive lifespans, where females cease to reproduce by the age of 30 - 40 years while continuing to live well to the age of 90 years (Bigg et al., 1990). Of females that survive past the age of 10 years 64 % continue to live a post-reproductive life (Nattrass et al., 2019).

For the grandmother effect to influence, inclusive fitness needs to be gained. Females need interaction with the grandoffspring as well as a way of increasing that grandoffspring's survival. Since offspring of *O. orca* do not disperse from their natal group, they give rise to close family groups of which the grandmother often groups with both the offspring and the grandoffspring. Grandmothers provide a survival advantage for their grandoffspring, especially when these grandmothers are post-reproductive. Grandmothers that are reproductive are not capable of providing the same amount of support as can a post-reproductive grandmother. Probably because reproductive grandmothers have offspring of their own to care for and therefore their movement and activity is limited, restricting them of being able to lead the pod (Croft et al.,2017). It might also be because they need to feed their calf and themselves and therefore cannot share the food with other kin (Nattrass et al., 2019). This would mean that the evolution of ceased reproduction would increase a grandmothers capacity to assist (Nattrass et al., 2019), supporting the grandmother hypothesis.

Post-reproductive females of *O. orca* are banks of ecological knowledge that carries over generations down throughout their leadership of the pod. This ecological knowledge is crucial, especially during low abundance of resources such as food, at least in resident *O. orca* (Brent et al., 2015; Croft et al., 2017; Nattrass et al., 2019). The fact that post-reproductive females of knowledge lead the pod might bear part of the explanation to why menopause has evolved in this species. The knowledge of the elders may be more comprehensive than that just of ecological, it might include social aspects as well (Brent et al., 2015).

4.1.4 Other species to which the grandmother hypothesis may be applied

Additionally, an odd display of the grandmother effect is that of the aphid *Quadrartus yoshinomiyai*. This social insect of *Q. yoshinomiyai* produces galls, a growing on external tissue of plants not produced by the plant itself, that provide nests rich in food that is worth defending against predators (Uematsu et al., 2010). They demonstrate patterns of non-random spatial distribution within open galls, where the first-instar nymphs (the founder) and wingless adults placed themselves around the hole of the gall and the reproductive older nymphs and winged adults placed themselves further in the gall, away from the hole (Uematsu et al., 2013). Examining the abdomen of adult *Q. yoshinomiyai*, the number of mature embryos in the abdomen reveals whether the adult is prereproductive or reproductive, which have shown that adult defenders are predominately post-reproductive. In fact, the wingless adults exhibit different aspects of resource allocation of survival, reproduction and defence. Uematsu et al. (2010) have shown that the wingless adults cease reproduction when the gall is mature and open and survive for a prolonged period. The shift of ceased reproduction to defence of wingless adult coincides with the time of ecological factors that require it, thus the opening of the gall. This shift is part of the resource allocation in response to the ecological factors. Wingless adults in closed galls contain a lot of embryos and less of waxy defensive secretion, while winged adults in open galls contain almost exclusively waxy defensive secretion. The abdomen of both these adults is of a similar size and shape, indicating resource allocation of aging adults of embryo production and secretion synthesis. This shows post-reproductive altruistic behaviour of indirect fitness benefits for *Q. yoshinomiyai*. Furthermore, this suggests that post-reproductive altruism does not necessarily evolve of the basis of intelligence (Uematsu et al., 2010). It seems that colonies of *Q. yoshinomiyai* maximize their

group phenotype by minimizing the cost of altruistic defence at group level by the value of reproductive colony members (Uematsu et al., 2013).

4.2 The mother hypothesis

The mother hypothesis first suggested by Williams (1957), states that the fitness of offspring depends on maternal care. In addition, states that increased mortality risk of reproduction leads to increased advantage in cessation of reproduction and investment in already born offspring, rather than prolonged reproduction with increased mortality for both mother and offspring. The cessation of reproduction enables females to increase their fitness at two levels in regard of the mother hypothesis. The first level being the survival of immature offspring, the second being the fertility of mature offspring. The first level of the mother hypothesis refers to the fact that offspring is dependent on maternal care in order to survive and the mother needs to stay alive in order to care for her offspring, the survival of the mother is essential for the survival of her offspring. Consequently, it might be beneficial to cease reproduction to reduce the mortality risk of her already born offspring and increase their survival to maturity. Menopause may thereby have risen by the first level of the mother hypothesis by the effect of a mother's death on the offspring survival and the mother's mortality risk of birth. Thus, increased age at birth decreases the probability of the offspring reaching adulthood while the mother is still alive, and thereby the contribution of late life fertility to fitness is lower. Therefore, there is always an age at which it is more advantageous to cease reproduction in favour of prolonged reproduction. This cessation of reproduction could have been positively selected for in the past if complications at birth would increase with increased age, given rise to post-reproductive life (Pavard et al., 2008).

According to Peccei (2001a) mothering is the origin of menopause. She points out the uncertainty of caring for grandoffspring as a basis of which post-menopausal life has evolved and points to Hamilton's law of grandmothers:

$$\frac{b}{4} > c \qquad (2)$$

And Hamilton's law of mothers:

$$\frac{b}{2} > c \quad (3)$$

She claims that even if there is truth to these and there is a decreased cost for grandmothers due to decreased fertility, in real life the gain in increasing the survival and fertility of one's own offspring is greater. Moreover, she claims that grandmothering might sustain menopause, but mothering is what triggered menopause. Since the first mother experiencing premature reproductive cessation would probably have had an offspring of her own to care for, still dependent on her, therefore mothering and not grandmothering is the basis of menopause. Because if prolonged fertility has a negative effect on mothers as well as the mortality of mothers have negative effect on juvenile survivorship, then premature reproductive senescence and the post-reproductive life of human females evolved by the assurance of prolonged care for the already born offspring. All of which, a response to mothering, not grandmothering (Peccei, 2001a).

4.3 The reproductive conflict hypothesis

4.3.1 The concept of the reproductive conflict hypothesis

A factor which is not considered in the previous adaptive theories, that might shed some light on the evolution of menopause, is that of inter-generational reproductive conflict. According to theories, the cost of reproductive conflict by females of different generations of shared social units is a missing component in classical inclusive fitness (Cant & Johnstone, 2008; Johnstone & Cant, 2010). The reproductive conflict is to a great extent affected by the age-specific relatedness among females which differs depending on the social structures of mating patterns (Johnstone & Cant, 2010; Lahdenperä et al., 2012).

The evolution of post-reproductive life may be explained, partially, due to relatedness. The relatedness depends on the age-specific changes in local relatedness, which changes with age in populations of overlapping generation (Johnstone & Cant, 2010; Lahdenperä et al., 2012). The concept of age-specific relatedness depends on the social structure as well as the demography.

Johnstone and Cant (2010) explain these structures as important factors affecting the age-specific relatedness. The predominant factors of social and demographic structures affecting age-specific relatedness are those of sex-biased dispersal and the mating system. Populations with non-local mating and female-biased dispersal increases the relatedness with age while populations with local mating or male-biased dispersal decreases relatedness with age, in both these examples the female-female relatedness is constant while the female-male relatedness varies. In a population of female-biased dispersal or non-local mating, the relatedness of males and breeding females increases with age. This is because the female has a low relatedness to males as she begins her life apart from her father and his relatives, either because she disperses or due to extra-group mating. As she breeds, she might produce sons of her own, increasing the relatedness of males in her social group but also increasing the relatedness of breeding males in local groups. In contrast, male-biased dispersal in a local mating population decreases the relatedness of males since she begins her life with her father and relatives and as she breeds, her potential sons disperse from the social group decreasing the relatedness (Johnstone & Cant, 2010). These social and demographic structure affecting the relatedness, further affect the intergenerational conflict (Johnstone & Cant, 2010; Lahdenperä et al., 2012), especially if overlapping reproduction occurs (Lahdenperä et al., 2012). By this there are two types of social structures of species that experience post-reproductive phases where the local relatedness increases with female age, social structures of female-biased dispersal and local mating in ancestral humans, as well as those of philopatry of both sexes with extra-group mating in *O. orca* and *G. macrorhynchus*. This increase in local relatedness makes the females of these social structures susceptible to the evolution of reproductive constraint and altruistic behaviour later rather than early in life. By this, social structure and dispersal patterns are factors relevant to the evolution of grandmothering and the menopause (Johnstone & Cant, 2010).

In populations of overlapping reproduction, the mortality rate for offspring increase, leading to intense competition mainly between in-laws. The extent of the conflict predominately affects the reduction in inclusive fitness in association with co-breeding, which in turn may contribute to selection against further reproduction in in age-structured populations. However, there seems to be greater survival rate for offspring of overlapping reproduction of relatives, compared to overlapping reproduction with in-laws which exhibit substantial lower offspring survival rate. Similarly, the difference in inclusive fitness of overlapping reproductive generations and non-

overlapping reproductive generations is only of significance in patrilocal, the males natal group (Lahdenperä et al., 2012).

Furthermore, Johnston and Cant (2010) explain the cost and benefits of the inclusive fitness approach that might occur in populations with these types of social structures. Such as, an action of a female of certain age (*a*) that entails an immediate loss of offspring (*c*) for that female, and an immediate gain of (*b*) offspring for others in that group. Where $b > 0$ it is referred to as helping behaviour, and where $b < 0$ it is referred to as harming behaviour. These actions affect the fitness of the local offspring by competitions for breeding possibilities. By applying these actions of costs and benefits as well as the age-specific relatedness to the different types of social structures, the selection strength of favouring helping contra harming behaviour in different ages is determined. Data show that in a population of either female-bias dispersal or non-local mating helping behaviour increases with age since female relatedness also increases with age. By helping the social group she simply helps her kin (Johnstone & Cant, 2010).

4.3.2 Reproductive conflict in form of suppression

A distinct form of reproductive conflict is that of reproductive suppression. Reproductive suppression is assumed to occur among humans (Wasser & Barash, 1983) and other mammals such as *G. macrorhyncus* (Kasuya & Marsh, 1984). During some forms of reproductive suppression female reproductive success can improve by manipulating other females' reproduction. The mechanism of reproductive suppression has probably been an important factor in our evolutionary past and might keep on being important. Temporal changes in reproductive success give rise to natural selection to act on, as age and its physiological changes. In terms of reproductive success and ageing the reproductive suppression is explained by $RS1$ being the present conditions and $RS2$ being the future conditions, all else being equal. Until a female reaches her prime age of reproduction, the future conditions should tend to be more advantageous according to:

$$RS2 > RS1 \tag{4}$$

As a female passes her prime age of reproduction the present condition should tend to be more advantageous than the future conditions according to:

$$RS1 > RS2 \quad (5)$$

By this, a younger female having greater reproductive success in future conditions ($RS2 > RS1$) should be more likely to delay her reproduction. Contrary to an older female that has greater reproductive success in present condition ($RS1 > RS2$) that should be less likely to delay her reproduction (Wasser & Barash, 1983). Social suppression may occur by females trying to enhance one's own reproduction by suppressing someone else's reproduction by manipulation. This may occur when conditions that are socially dependent affect the reproductive success. It is beneficial for females to suppress other females' reproduction in terms of socially dependant resource availability. Manipulating someone else's time and frequency of reproduction may thereby improve their own reproduction. Low self-esteem and lack of social support among western women are associated with reproductive complications such as infertility, spontaneous abortions and complications during and following birth. These are states that may be the outcome of harassment of other females and indeed come to reproductive suppression. If the competition is high and the social harassment is frequent it might be beneficial for the harassed female to suppress her own reproduction, until future conditions are less competitive and more beneficial. When favouring someone else's reproduction by suppressing the reproduction of oneself, the effect of relatedness influences. In a group of closely related females, younger and older females should be more likely to suppress their reproduction by increased inclusive fitness (Wasser & Barash, 1983).

Reproductive suppression is thereby either a result of increasing the inclusive fitness by enhancing kin reproduction by suppressing one's own reproduction, or by non-kin suppressing their own reproduction and aiding in hopes of becoming the dominant breeding female. Both suppressing one's own reproduction and suppressing someone else's reproduction has its benefits (Wasser & Barash, 1983).

4.3.3 Reproductive conflict among humans

The selection to minimize the reproductive competition between generations of the same social units has probably predominately shaped the human fertility. Humans have an exceptionally low level of reproductive overlap, which means that females only reproduce during a fraction of their daughter's reproductive lifespan, even though they live long past that period. The fact is that the age of females in natural-fertility populations where the competition of reproductive females of the next generation begins, coincides with the start of the reproductive senescence. The nature of this pattern is due to the female-biased dispersal that ancestral humans presented (Cant & Johnstone, 2008). In most other vertebrates where competition of reproduction has led to evolutionary separation of reproductive generations, the older generation maintain the reproductive status (Hill & Hurtado, 2012; Wasser & Barash, 1983). The effect of reproductive conflict by female-biased dispersal can be explained by an equation of relatedness, for grandmothers:

$$(1 - p)/4 \qquad (6)$$

A newly dispersed female to her male natal social group has no relatives. She can either breed an offspring of her own of which the relatedness is of ½, or she can recede from breeding and assist an older female of the social group (the mother of her mate) of which the relatedness is none. Therefore, the difference in relatedness of the two offsprings is ½. Similarly, the older female (the mother of the male) can either breed an offspring of her own of which the relatedness is ½ or she can assist the reproduction of her grandoffspring of which the relatedness is $(1 - p)/4$, where the relatedness is ¼ and p is the probability of extra-pair paternity. This means that if there is a chance that the son of the older female has fathered the offspring $p < 1$ and the difference between an offspring of breeding and that of helping the younger female is lower for the older female than for the younger female (Cant & Johnstone, 2008). Therefore, the younger female has an advantage since she has a great benefit of breeding an offspring compared to none of helping the older female, whereas the older female benefits from both situations however less from assisting her grandoffspring(Cant & Johnstone, 2008; Hill & Hurtado, 2012). The redistribution of reproductive investment from older to earlier throughout female life-history has surely increased the advantage

of younger females in reproductive conflicts, boosting selection of early reproductive cessation and separation of reproductive generations (Cant & Johnstone, 2008). However, the reproductive success of females must consider assistance from others, especially provisioning males, even though they state that older females assisting younger favoured by evolutionary pressure probably lead to promoting and maintaining the menopause (Hill & Hurtado, 2012).

4.3.4 Reproductive conflict among Orcinus orca

Reproductive conflict is displayed among *O. orca* where the mortality hazards for calves of older females is 1.7 times greater than calves of younger females (Croft et al., 2017). Among *O. orca* mating occurs non-local and neither males or females disperse from the natal matrilineal group, exhibiting high philopatry (Bigg et al., 1990). Johnstone and Cant (2010) concept of different relatedness with age is applied to *O. orca* by the social structure of philopatry for both sexes and mating outside of that natal group, as such the female-male relatedness increases with age (figure 2). Interestingly, the peak of relatedness for females coincides with the age of reproductive cessation (Croft et al., 2017). It is obvious that Johnstone and Cants (2010) model of predicting age-specific relatedness is indeed correct. However, it is also explicit that their model is lacking in predicting the decline of relatedness that follows a certain age, as in in *O. orca* where males rarely live beyond the age of 30 (Croft et al., 2017).

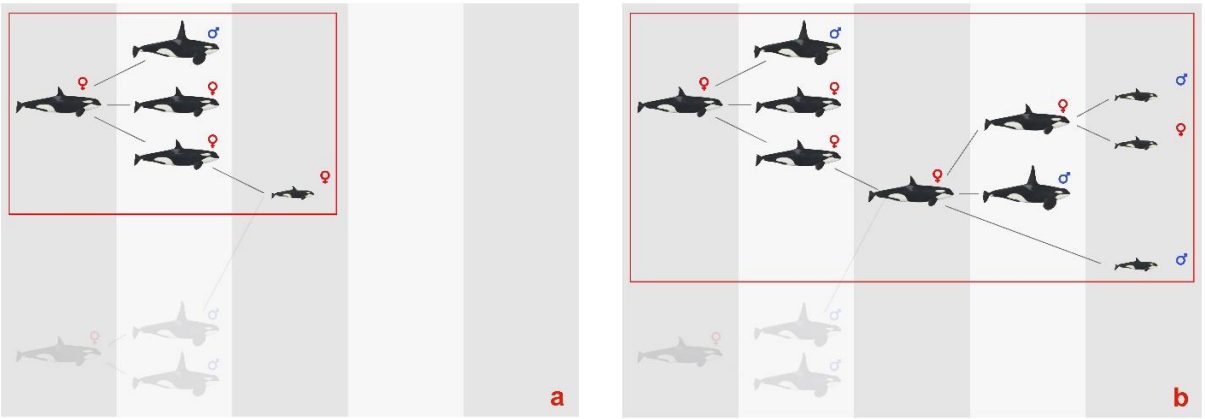

Figure 2. A simplified illustration of the local age-specific relatedness. By the social structure of philopatry of both sexes and non-local mating the relatedness increases over time. The red line indicates a certain local age-specific relatedness during a given age for an individual. The local age-specific relatedness for a juvenile (a) and the local age-specific relatedness for the same individual as an adult (b). In both a and b the father and his relatives of the social group is excluded since the mating occurs non-local and offspring is born into the mothers social group.

The reproductive conflict among *O. orca* has been evaluated based on the kinship dynamics which showed that in the so called "whale case" of competition, efforts and fecundity rate decreased with age. This shows that lower level of competition is favourable for older females. The reason that the "whale case" is significant is because the older females can maximize the inclusive fitness by caring for the kin due to the system of non-local mating. This means that the "whale case" live in natal social groups, compared to the so called "ape case" where there still is competition among the young. This risk of inter-generational conflict combined with the fact that offspring of *O. orca* rely on their mothers for a long period of years puts older females of reproduction in a substantial cost. In addition, first-born calves suffer a higher mortality rate than do siblings of a first born, this is probably due to the benefits of alloparental care, the care of additional adults that are not the parents. However, first-born offspring born into reproductive conflict by younger females experience higher survival than those born without reproductive conflict. Croft et al. (2017) argue that this is due to the grandmother effect, especially in times of scarce resources the benefits of leadership is valuable. Therefore, it seems as though co-breeding is beneficial for both younger females and older females, as the calves of younger females increase in survival rate and the direct fitness cost of older females is greater than the indirect fitness benefits of co-breeding (Croft et al., 2017). Johnstone and Cant (2010) claim that females would help sons to a greater extent due to the increasing relatedness to males and the increasing competition of reproductive resources between females. As well, Brent et al. (2015) suggest that post-reproductive females assist sons over daughters since they have a greater reproductive capacity to increase kin as well as this decreases reproductive competition with her daughters in her social group. The study by Croft et al (2017) shows this by observations of post-reproductive females that lead their sons, as well as the study of Foster et al. (2012). Sons experience greater mortality hazard when their mother dies, regardless of the sons age, suggesting that sons are more dependent on the leadership and support of the mother than daughters are (Brent et al., 2015; Foster et al., 2012). The mortality hazard is in fact greater for sons above 30 years of age than of those younger (Foster et al., 2012). This suggests a key factor of the evolution of early reproductive cessation due to inter-generational conflict by the atypical demography of *O. orca* (Croft et al., 2017).

5. *Non-adaptive theories*

5.1 Antagonistic pleiotropy

5.1.1 The concept of antagonistic pleiotropy

Selection will favour reproductive benefits early in life even though this early-life benefit has a negative impact in late-life reproduction. According to theories of antagonistic pleiotropy the menopause is the product of physiological trade-off of enhancing early-life reproduction by the cost of disadvantageous late-life reproduction (Peccei, 2001a, 2001b; Wood et al., 2000).

The theory that menopause simply is a product of antagonistic pleiotropy is not as widespread as the grandmother hypothesis and in some cases antagonistic pleiotropy is included as a factor in the grandmother hypothesis (Peccei, 2001a) as well as other hypothesis. Contrary to this some claim that antagonistic pleiotropy is a theory of its own. Wood et al., (2000) suggest that menopause is the end point of a decades-long follicular depletion rather than an adaptation, and that menopause has evolved by antagonistic pleiotropy. Accordingly, follicular depletion should thereby be beneficial early in life and selection carried out even though it might be disadvantageous in late life. They mean that the entire follicular-depletion system is the relevant phenotype for evolution, since this is an essential regulation of reproduction regardless of age. The follicular depletion is a continuous process from birth to the menopause, being the endpoint. This suggests that menopause is an artifact of early life processes that is beneficial and enhancing survival early in life. By this, the authors claim that the grandmother hypothesis is an unnecessary explanation for the evolution of menopause (Wood et al., 2000). Accordingly, Peccei (2001b) means that post-reproductive life is the product of the favourable mechanism of physiological trade-off of early reproductive cessation. Likewise, another study by Peccei (2001a) supports the mother hypothesis rather than the grandmother hypothesis by the selection for early fertility by antagonistic pleiotropy.

Might menopause be of adaptation due to that selection favoured post-reproductive life or might menopause be of epiphenomenon due to selection for effective early reproduction or the physiological restraint preventing prolonged fertility in increased longevity? Thinking in three terms is needed: adaptation, trade-off and constraint. Peccei (2001b) means that these three views

are overlapping and interacting, all playing a part in the evolution of menopause. She claims there is no evidence for the theory that the recent increase in lifespan is the basis of menopause, but that selection favours early fertility and reproduction might explain the physiological trade-off (Peccei, 2001b).

5.1.2 Antagonistic pleiotropy among humans

Among humans, the weak influence combined with several shortcomings of the grandmother hypothesis (described under 4.1.2) supports that the menopause is a product of trade-off rather than an adaptation. The implication of the recent increase in longevity of humans, indicates longer juvenile period and longer dependence on the care of mothers. By this, the menopause is rather a byproduct of increased longevity than an adaption, since the increased lifespan has given rise to prolonged dependence of juveniles as shown by increased developmental of cranial expansion which in turn promotes prolonged lifespan (Peccei, 2001a).

5.1.3 Antagonistic pleiotropy among Globicephala

As the perspective of the differences between *G. macrorhynchus* and *G. melas* in regard of post-reproductive life or not, one aspect is that of mortality rate. The mortality rate acceleration between these two closely related species, as well as *O. orca*, varies and the difference in mortality rate acceleration may therefore have given rise to different life histories of *G. macrorhynchus* and *G. melas* since they diverged. The basis for this difference in mortality rate acceleration might be because the selection for somatic repair and the selection against deleterious mutation accumulation and/or pleiotropic genes with deleterious late-life effects are expected stronger in late life among *G. macrorhyncus* and *O. orca,* than among *G. melas.* By this it seems as the evolution of post-reproductive life depends, partially, upon the survival until late life of females (Foote, 2008).

6. Discussion

6.1 Menopause and post-reproductive lifespan

In terms of defining the menopause there does not seem to be any differences regarding the menopause as the process of reproductive senescence, and when the cessation of reproduction is complete the post-reproductive lifespan begins. Even though menopause is a concept applied quite exclusively to humans, and the term post-reproductive lifespan is used more widely. As of the problematic approach of measuring post-reproductive lifespan is somewhat bypassed throughout the new measuring of post-reproductive representation, which considers post-reproductive life as a population trait rather than an individual. Post-reproductive representation will certainly elucidate the true amount of post-reproductive species or populations there truly are.

6.2 Adaptive theories

The weak influence of the grandmother effect found by Hill and Hurtado (1991) is probably true, keeping in mind that their study is based on one population of indigenous people studied for a time lapse of only 10 years. Even though a study of 10 years is a long period of time, it does not cover a human lifetime and certainly not several generations, which most often is necessary in evolutionary studies. Also, since the study was conducted on only one population there are few replicates, of which none probably are independent. Even if we could know for certain that their conclusion was completely true, that would still only apply for humans. The social structure for humans and other species, like *O. orca*, differs greatly and that is still only what we as humans can see, perceive and measure. To this extent the grandmother effect seems to have a greater effect in their social structures and might have an even bigger impact than we can know. Keep in mind that individuals of species like *O. orca* stay by their mothers' side in their natal group throughout their entire lives (to much of our knowledge, there might be varieties between ecotypes), which includes siblings, nieces and nephews as well, living together as a pod. This is however something Hill and Hurtado (1991) mention as parameters that would tip equation 1 to the beneficial side. As Hill and Hurtado (1991), Pavard et al (2008) doubt the influence of the grandmother effect, claiming that

in order to have a significant effect grandmothers would have to be the main care-givers, replacing the mother, the father and other relatives. Which probably also is true regarding humans but however not *O. orca*, yet this depends on the species and the demography.

In addition to the problems of small sample size and relatively short study period mentioned above, an additional flaw is the fact that one of their studies was carried out on Ache hunter-gatherers with a social structure of female dispersal and local mating. That is not the universal case of social demography, as it differs among species and populations. In species like *O. orca* the social dynamic constitutes of philopatry for both sexes and non-local mating, which entails that kinship increases with age for females. This may mean that the grandmother effect is greater in species with social dynamics and mating patterns as *O. orca* (Johnstone & Cant, 2010) and probably *G. macrorhyncus* as well.

The social dynamics of *O. orca* entail that only grandoffspring of granddaughters is brought up in the natal group. As both sexes are philopatric and there is non-local mating this means that the offspring of a male is brought up in another social group. However, among this species there is evidence that females assist their sons predominately. This would mean that females invest more in sons which does not provide grandoffspring to the natal group, but instead to another family group. A possible explanation might be that investing in sons rather than daughters will ensure the dispersal of genes in pods other than their own. Another reason might be that investing in sons predominately alleviate possible inter-generational conflict to some extent.

The importance of possible confounding factors that may impact the grandmother effect I think is important, since we just cannot overlook some frequently occurring factors. Of course, different factors influence different situations, and these factors I think need to be modified accordingly. As an example, ignoring the presence and impact of fathers and grandfathers among perhaps humans in terms of evaluating the grandmother effect generates a false actuality. However, the same scenario among *O. orca* there are no need for evaluating the role of fathers and grandfathers because they simply are not present. In accordance, Peccei (2001a) introduces some good points in regard of lack of the grandmother hypothesis, such as evidence for universal grandmothers as caretakers as well as other caretakers besides grandmothers, and the need for female philopatry in order for the grandmother hypothesis to have effect among others. Most of these need to be taken

in consideration. There are more species than humans, to some of them these points do not fully apply and to some they might and it probably depends on a variety of factors. The need for extended maternal care obviously, the social dynamics of group pattern, dispersal pattern, mating pattern, conflict and kinship dynamics. These factors may not cover an explanation, but how about the life-history artefact? What did the species societies look like hundreds of thousands of years ago, what may have led to the lack of assisting kin or prolonged care for offspring? Is it all about quantity over quality? Theories suggesting that the cessation of reproduction has evolved due to the vital role of extended maternal care is according to Hawkes et al. (1998) rightfully doubtable, due to the fact that there are primates of which extended maternal care is vital. However these primates lack the early cessation of reproduction. Yet, it is most sensible that post-reproductive life emerged from the need for extended maternal care. Both the evidence and the lack of evidence for the grandmother hypothesis I believe is rightful. Pointing to the evolution of menopause by simply one theory is not enough. Instead an integrated approach of theories taking into account the parameters of which the species or populations live by.

The two levels of the mother hypothesis, with the grandmother hypothesis in mind, seem more reasonable to divide among mothering and grandmothering such as the first level is provided by the mother and the second level is provided by the grandmother. Depending on the species, it is not unreasonable and perhaps even a common care for the offspring of both mother and grandmother. Such common care is exhibited by species like *O. orca* and should therefore not be excluded. According to Hill and Hurtado (1991) the mother effect varies between populations, which should influence the grandmother effect as well. Indeed, if all mothers were to be flawless mothers in every aspect there would never be any need for grandmothering and they would perhaps invest in prolonged reproduction of flawless motherhood.

In accordance, there are studies supporting the grandmother hypothesis among *O. orca,* yet it seems as the prolonged care for offspring by this species supports the mother hypothesis as well. The fact that offspring stay in their natal group throughout their lives sharing food with their grandmothers and the fact that the mortality rate increases significantly when a mother passes, especially for sons, suggest the influence of both the grandmother effect and the mother effect. How about a scenario where young and breeding females, the mother hypothesis is applied and

they care only for themselves and the offspring. While older and post-reproductive females care for their grandoffspring after the initial care of the mother, showing and sharing the knowledge of survival. If so, then the evolution of post-reproductive life and the maintenance of it is certainly possible by both mothering and grandmothering. Observing *O. orca* which care for their offspring alongside caring for their grandoffspring in their older age, this is apparent. Regardless, the display of both grandmothering and mothering among *O. orca* would generate fitness benefits of one's owns reproduction as well inclusive fitness by caring of grandoffspring, optimizing the fitness.

By this, it seems reasonable that the post-reproductive life should have evolved by mothering rather than grandmothering, since mothering is the basis of reproduction and upbringing of offspring, and the costs by late reproduction increase with age. Yet this as well depends on the social structure of the species or population in mind.

The reproductive theory seems indeed to be part of the missing puzzle of the origin of menopause. The evidence suggest that demography is an essential factor, as well as age-specific relatedness of kinship dynamics, which depends upon the demography of social structure. Further, it seems as though overlapping reproductive generations might have given rise to post-reproductive life by two paths. Thus, both co-breeding and inter-generational conflict favour early cessation of reproduction. As exhibited among *O. orca,* the matrilineal female, the grandmother, leads the pod to prosperous hunting grounds, and her role is of great importance during difficult times as of food shortage. In these societies the concept of co-breeding, or perhaps suppressing one's owns reproduction in favour of inclusive fitness, seems to be the general way of life. The significant difference of inclusive fitness of overlapping reproductive generations in patrilocal populations indicate the difference of reproductive conflict among related and non-related females.

No doubt reproductive suppression occurs among social groups, which as well depends on the social structures. The distinction between reproductive suppression and reproductive decline due to extrinsic factors should be difficult. Especially in the case of self-implied reproduction suppression and ecological factors that may influence the decision of suppressed reproduction, since I would imagine there would be a correlation between reproductive suppression and lack of resources.

As in the case of the grandmother hypothesis, the same should apply for the reproductive conflict hypothesis. That is, different factors influence different species and populations and I think it differs greatly and that demography is essential in understanding the social dynamics and evolution of menopause by reproductive conflict.

6.3 Non-adaptive theories

The existence of antagonistic pleiotropy and trade-off is a universal feature for certain and reoccurs among different theories of the evolution of menopause. I do not think there is a distinction between antagonistic pleiotropy as a theory and other evolutionary theories for menopause, but rather antagonistic pleiotropy is in some sort present in all theories.

Peccei (2001a) wrote that post-menopausal women should not suffer any negative consequences beyond that of normal age-related deterioration if menopause simply was meant to enhance female fitness. I do not find that likely to be true, and I think this notion suggests to the antagonistic pleiotropy. As with almost everything there are favourable and disfavourable aspects. A favourable trait in a situation might be disadvantageous in another situation and the balance between them gives rise to selection for or against them, which in turn might lead to a trade-off. So, menopause enhancing female fitness does not come without a cost, especially if menopause has evolved due to inclusive fitness. Decoupling antagonistic pleiotropy from evolutionary theories to declare it a separate theory is unreasonable, but instead considering antagonistic pleiotropy as an influencing factor among the evolutionary theories.

7. Conclusion

There is not one right theory while all the others are untrue, no absolute explanation for the evolution of menopause. Species, and sometimes populations, differs with respect to a range of characteristics. The degree to which the different theories for the evolution of menopause apply therefore probably also varies between species. Furthermore, a widespread array of factors

influences these theories and is therefore important to consider. It seems as though it is a puzzle inherently to put together the variety of factors and theories appliable to one specific species or population alone. Among the most essential factors is the demography of the social structure as the patterns of mating and the kinship dynamics.

Accordingly, Nattrass et al. (2019) mean that we simply cannot explain the menopause by either the grandmother hypothesis or the reproductive conflict hypothesis, but rather by applying an integrated approach which consider both the fitness benefits of post-reproductive females assisting and the costs of late-life reproduction. There are many theories and they all seem reasonable enough, depending on the species and the influencing factors such as social structure and the dynamics of kin. As for the theory of antagonistic pleiotropy I believe plays an important role not as a theory by itself, but as an underlying factor of life.

The grandmother hypothesis may not be adequate to explain the evolution of menopause among humans, but the fact remains that it is not the case among other species. The grandmother hypothesis has shown strong among *O. orca*, and the reason to why post-reproductive life has evolved predominately among species of Odontoceti is probably due to their demography of social and kinship structures. Thus, rejecting the grandmother hypothesis on account of studies carried out on other species is wrong. This shows the crucial fact that different theories are unequally appropriate on various species or populations. As such, needs to be considered consciously.

Consequently, an integrated approach considering the specific demography and factors for populations or species along with the hypothesis is needed in order to evaluate an adjusted model of the evolution of menopause.

8. *Societal and ethical considerations*

Increased knowledge and understanding of the origin of menopause and the distribution amongst species may enable the reduction of menopausal symptoms among women suffering from them. Ethical precautions in the future might be in regard of handling other species.

No ethical considerations were needed to carry out this part of the study. However, ethical questions regarding all the studies of which this paper is based upon might have been needed, especially if there where field studies or laboratory work with test animals.

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