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Twinning as an Evolved Age-Dependent Physiological Mechanism: Evidence from Large Brazilian Samples

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Additional information is available at the end of the chapter

Abstract

Multiple pregnancies occur in humans and other primates, which indicate that the twinning propensity is phylogenetically old. Factors such as decreased sexual dimorphism and size, rich and diverse nutrition and paternal care are related to multiple pregnancies in other animals. In human populations, despite its costs, twinning has a genetic basis and in Europe, Africa, and America, it was found that it increases mothers' fitness. Here, we explore the hypothesis that twinning represents an evolved physiological mechanism, particularly in mothers of higher age, as an 'all-or-nothing' last chance strategy for reproduction just before menopause. We present decade-long, large-scale population data about maternities from the city of São Paulo and the entire country of Brazil that indicate a considerable main effect of advanced age in promoting twinning, particularly dizygotic (DZ) twinning, but also monozygotic (MZ) twinning and higher order maternities. We also show that socioeconomic status is an important contextual factor increasing twinning. Besides the theoretical implications, these datasets establish a Brazilian countrywide twinning rate of 9.39‰ and highlight an increasing historical trend. This chapter promotes the importance of integrating proximate patterns from human and nonhuman animals and evolutionary factors in order to reach a comprehensive view about twinning.

Keywords: twinning rates, age dependence, physiological mechanism, evolutionary theories, population data, socioeconomic status

1. Introduction

Multiple pregnancy, the gestation of two or more embryos at the same maternity, regularly occurs in humans and other primates, which indicates that the twinning propensity is phylogenetically old within the order of primates. Despite the general pattern within the primate order of having single infant litters, multiple births occur in a number of species. The occurrence of twinning has been described, for instance, in chimpanzees (*Pan troglodytes*) [1–3], gorillas (*Gorilla gorilla*) [4, 5], orangutans (*Pongo pygmaeus*) [6, 7], vervet monkeys (*Cercopithecus aethiops sabaeus*) [8], macaques (*Macaca fuscata*) [9] and (*Macaca thibetana*) [10], capuchins (*Cebus apella*) [11, 12], marmosets (*Callithrix jacchus*) [13, 14], and also in prosimians, such as pygmy loris (*Nycticebus pygmaeus*) [15], lemurs (*Lemur catta*), and galagos (*Galago crassicaudatus argentatus*) [16]. As the last common ancestor between prosimians and humans (and all other primates) lived approximately 75 million year ago [17], the tendency toward twinning in primates has deep-seated biological roots. Furthermore, the existence of higher order litter size in other mammals [18] suggests that phylogenetically speaking, twinning is an even older propensity.

Comparative studies have identified some general factors related to increased litter size. Carranza [18] analyzed 106 species of mammals and, controlling for body mass, he found that increased sexual dimorphism is linked with decreased number of offspring per litter. It was also found that higher body mass is related to reductions in litter size, but only among larger mammals. Within primates, multiple births are limited to the smallest species [19]. Chapman et al. [20] analyzed factors related to multiple births in 70 species of primates and found that twinning primates tend to be small, have short gestation periods and give birth to small infants that are weaned quickly, and mature rapidly. They also tend to be commonly insectivorous, which they argue would allow a relatively high metabolism facilitating large litters. The authors suggest that adopting a more diverse diet containing not only fruit, but also insects could ensure access to nutritional resources that are not restricted seasonally or by the presence of toxins. Finally, they determined that litter size among species with paternal care was significantly higher than that of species with no paternal care. This is especially true for marmosets which they claim have the best 'package deal' for twinning: small body size, monogamy (or polyandry), and paternal care. Aligned with this, Stockley and Hobson [21] analyzed 427 mammalian species and found that increases in offspring production follow the evolution of paternal care, specifically where males contribute with investments, such as food provisioning for young. Therefore, there is an overall pattern relating to decreased sexual dimorphism and size, rich and diverse nutrition, and higher paternal care to increase litter size in primates, and in mammals in general, which should be taken into account when focusing on humans.

In Brazil, two cases of twins in capuchin monkeys (*Sapajus libidinosus)* were observed in a free wildlife setting in *Fazenda Boa Vista*, south of Piauí State (Northeast, Brazil). Comparing these cases with two other populations of capuchin monkeys in Brazil (*Parque Estadual Carlos Botelho* located in São Paulo State and *Reserva Biológica de Una*, located in Bahia State), the one in Fazenda Boa Vista presented the lowest offspring interval, and was attributable to more food availability in this region (Izar, Fragaszy & Visalberghi, personal communication) [12]. Capuchin monkeys feed on fruits and invertebrates (**Figure 1**) and also help to care for the offspring of others (**Figure 2**).

Figure 1. On the left, a female called 'Piaçava' carrying two female twin daughters: 'Paçoca' and 'Pamonha', 2009. On the right, the female twins Paçoca and Pamonha, from the 'Chicão' group. Photographed by Elisa Visalberghi.
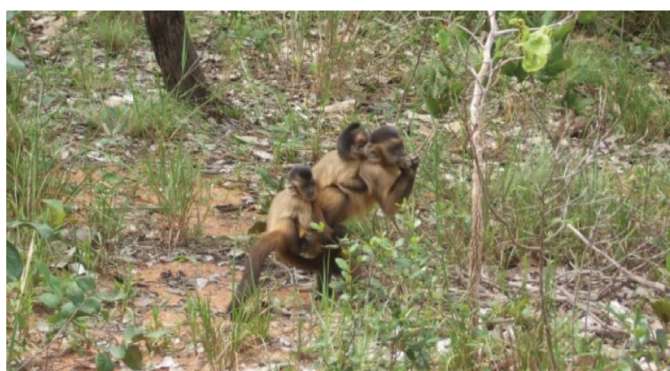

Figure 2. Twins carried by older female sister, *S. Libidinosus*, 2009, from 'Zangado' group. Photographed by Luiz Carlos M. Biondi.

1.1. Twin birth in the closest living relatives of humans

Chimpanzees are the closest living relatives of humans. The mean divergence estimation date between humans and chimpanzees is 7.65 ± 1.01 million years ago [17]. Therefore, from an evolutionary perspective, the comparison of humans with chimpanzees is especially interesting. Ely et al. [1] analyzed multiple births in chimpanzees using a database of 1,865 maternities recorded in the security, stability, and abundance of captivity (five different colonies) over a 76 years period from 1926 to 2002. When we compare the results from Ely et al. [1] to the corresponding Brazilian twinning rates from the city of Sao Paulo [22], we see that monozygotic (MZ) twinning rates were virtually the same comparing chimpanzees (4.3‰) and humans (4.42‰). However, dizygotic (DZ) twinning rates were more than three times higher in chimpanzees (23.6‰) than in humans (7.15‰). Similarly, higher order multiple birth rates

were almost three times higher in chimpanzees (1.1‰) than in humans (0.36‰). Chimpanzee females that had given birth to twins were five times more likely to give birth to twins in a subsequent pregnancy in comparison with those who delivered singletons. Among humans, recurrence rates of twinning in a subsequent birth increase 2–3 times [23].

Among wild chimpanzees from 135 maternities recorded between 1965 and 1994 in the Mahale Mountains National Park, one birth of newborn twins was observed [24]. The twins' mother seemed overwhelmed and walked less than usual [2]. She stopped frequently to rest after walking 10–20 m. Whereas single newborn infants seldom vocalize, the twins exhibited a high frequency of vocalizations (5.8 per minute). During resting, both sometimes fell from her lap and uttered loud cries. The twins' mother had nursed her first single infant, but she did not nurse the newborn twins in spite of their nipple-rooting behavior. The explanatory hypothesis raised was insufficiency or absence of milk flow. After 1 week, the twins had disappeared. In the Gombe Stream National Park, one birth of newborn twins occurred in 59 recorded pregnancies [25, 26]. One of the twins gained weight and survived, but the other died when he was 10 months old. It is noted that even in captivity, 64% of the chimpanzees born as twins die during the first year of life. The mortality rate among singletons during the same period was only 23% [27].

At the Noichi Zoological Park, during a 1-year period, interesting observations of alloparenting behaviors toward a 2-year-old twin chimpanzee were made [28]. Alloparenting is defined as care provided by individuals other than the mother. Two adult females affiliated with the mother engaged in the same kinds of parenting behavior as the mother directed toward a female twin (walking, infant carriage, grooming, and physical contact). The father was mainly engaged in walking together, physical contact, and playing with the male co-twin. Alloparenting may have contributed to the successful rearing of these twins. Three years corresponds to the middle of infancy in the chimpanzee life cycle and the infants are still dependent on adults for transport during travels, but 2–3-year-olds already depart from their mother and make requests to other adults. Alloparenting in chimpanzees increases survival of the offspring, even twins, and decreases birth intervals [28]. Such results may explain coevolution of the relatively short birth intervals among humans and origins of human alloparenting institutions (e.g., nursery school).

Chimpanzees wean their single offspring at an average of approximately 5 years and the interbirth interval is about 4–5 years [29, 30]. Observations made at the Kibale National Park, Uganda showed a significant negative association between the speed at which chimpanzee females weaned their infants and the amount of alloparental care received [31]. The contribution of milk to infant diets, evaluated through fecal stable nitrogen isotopes, was lower when the infants received more alloparental care. This may benefit females enabling them to invest sooner in a subsequent offspring.

Alloparental care may have been significant in shaping human evolutionary history. Analysis of the dataset from the standard cross-cultural sample showed that the average age at weaning singletons for 58 traditional societies was 31 months [32]. Age at weaning tended to be about 6 months lower in societies in which allomothers helped with child care, compared with societies in which the burden of child care was on the mother alone. Alloparental care

was also correlated with shorter birth intervals [33, 34]. It has been estimated that during their lifetime women reduce their child-care effort by 14–29%, in comparison with other mammals, due to the child care support they receive [35]. Menopause, which is present in humans and to some extent in nonhuman primates [36], is considered an adaptation that enables grand-maternal care, also contributing to a higher birth rate [37]. Sear and Mace [34] found that the death of the mother was clearly associated with high child mortality in 45 traditional societies they studied, especially when the mother died in the first year of the child's life. Examining whether the presence of kin affects child survival rates, they found that maternal grandmothers and siblings tended to improve child survival rates. Both fathers and paternal grandmothers showed somewhat more variation in their effects on child survival.

1.2. Twinning as an adapted propensity

In human populations, twinning is universal and a relevant part of cultural life, mythology, religion, and art [38–40]. There are documents on occurrences of twinning in historical populations, such as in seventeenth to eighteenth century French Canadian immigrants [41], or in eighteenth century Sweden [42]. Further, hereditary factors influence the propensity for twinning [39], typically DZ twinning [43, 44], although there is also some evidence for genetic influence on MZ twinning [45, 46]. For instance, in Brazil, one study found two genetic polymorphisms, TP53 Pro72Arg and MDM4 rs1563828, to be associated with twinning [47].

Twin pregnancies, especially monochorionic that are mostly MZ [39], are risky (e.g., adverse effects include twin-twin transfusion syndrome, twin anemia polycythemia sequence, selective intrauterine growth restriction, twin reversed arterial perfusion sequence), calling for increased medical and societal attention (e.g., [48, 49]). The chance of maternal mortality associated with multiple pregnancies is higher in comparison with singleton pregnancies. When one fetus dies, there is an increased risk of preterm delivery, neurological sequel, and co-twin death (Elito Jr., this volume).

Landy and Keith [50] used the expression *vanishing twin syndrome* (VTS) to refer to fetal resorption during the first months of gestation, thereby reducing a twin pregnancy to a singleton pregnancy, a phenomenon originally described by Stoeckel in 1945. In the past, this occurred without women's knowledge, but with the use of ultrasonography fetal resorption is more frequently diagnosed. Monitoring 228 twin pregnancies after natural conception, Márton et al. [51] reported an incidence of vanishing twin syndrome in 18.2% of twins, although it varies considerably, from 0 to 100% [39].

Despite all the costs and risks involved, the confluence of twinning's widespread occurrence, deep phylogenesis, universality, antiquity, and genetic basis point to the possibility of its important adaptive relevance in human evolution. Indeed, in contemporary Africa, Europe, and America, it was found that twinning increases mothers' fitness, that is, number of surviving offspring (e.g., [52–55]). Sear et al. [55] analyzed a database of 3,136 births, between 1950 and 1974, of a natural fertility population in rural Gambia, before the establishment of medical service. Fertility and mortality were also high in this population. The twinning rate was 15.9‰ (50 twin maternities). Twin mothers had higher fertility, shorter interbirth intervals, and later age at the last reproduction than their singleton-only bearing

counterparts [55]. Therefore, the higher fertility of twin mothers outweighs the higher mortality of twins, indicating a fitness advantage of twin mothers in comparison with singleton mothers.

In the USA, Robson and Smith [54] accessed the Utah Population Database and compared the reproductive and survival events of 4,603 mothers who bore twins and 54,183 who bore singletons. These mothers were born between 1807 and 1899, lived at least to the age of 50 years and married once. They found that mothers of twins presented a robust phenotype, exhibited lower postmenopausal mortality, shorter average interbirth intervals, later ages at last birth and higher lifetime fertility than their singleton-only bearing counterparts. Beiguelman et al. [56] and Tagliani-Ribeiro et al. [47] also found that Brazilian twin mothers have a higher number of pregnancies than controls. Thus, because longevity and fecundity are increased in mothers of twins, the twinning propensity can offer some payoffs in terms of higher differential evolutionary fitness.

There are many evolutionary theories about twinning; however, here we outline two key hypotheses. The *insurance ova hypothesis,* proposed by Anderson [57], considers twinning as a by-product of selection for polyovulation, a mechanism which increases release of more than one oocyte per fertile phase of menstrual cycle due to multiple follicular development, promoting fertility and counterbalancing embryo defects and high spontaneous abortion rates. This event is associated with higher FSH concentrations induced by the decreased negative feedback mechanism reaching pituitary, which overshoots the threshold of ovarian follicle response in advancing maternal age [58]. In short, this hypothesis explains dizygotic twinning as an insurance mechanism against spontaneous abortion caused by both genetic and nongenetic defects. Apparently, the insurance ova hypothesis only explains higher rates of dizygotic twinning in older mothers. Ball and Hill [59] extended this hypothesis with their *insurance ova/pre-implantation selection model.* They agreed with Anderson that dizygotic twinning may be a by-product of selection for multiple ovulations. As such, multiple ovulations reduce the risk of embryo defects and conception failure. They went on to show that genetic defects covary with twinning rates across 24/25 countries; Nigeria, which has a unique biology when it comes to twinning, was the sole exception.

Forbes [60, 61] proposed an evolutionary explanation focused on relaxed maternal screening to eliminate genetically abnormal embryos—the *relaxed-screening hypothesis*. This screening system regulates both offspring quality and number; however, he argues that this system seems to falter in older mothers. He explains as a manifestation of this screening system the fact that twinning is two to four times more common at conception than at birth, hence the vanishing twin syndrome. The relaxed-screening hypothesis proposes an evolutionary framework in which the uterus of older mothers should become 'less selective' about offspring quality/quantity. He proposes two pathways for how this might happen. One is that as the mother approaches menopause, low quality offspring are better than no offspring at all. Another explanation is a maternal strategy to enhance the likelihood of carrying a normal pregnancy to term as a mother approaches menopause. This is plausible, given the conservative nature of the screening in which some healthy offspring are normally eliminated along with abnormal offspring. Thus, Forbes [60, 61] suggested that the maternal age increase in

twinning rate arises not only from a greater frequency of poly-ovulation, but also from elevated embryo survival, in general, regardless of its origins from one or two zygotes, because of the relaxed screening. Therefore, even though initially not made explicit by Forbes [60], the relaxed-screening hypothesis explains higher rates of dizygotic and monozygotic twin births in some mothers approaching menopause. Interestingly, one MZ pair in a recent case of doubly exchanged MZ twins was born to a mother age 45 years [62]. It has been suggested that aging ova may lack certain sources of nutrition and energy, leading to delays in development and errors in the programming of some cells, which in turn result in the initial splitting of zygote that results in MZ twins [39, 62].

These two evolutionary hypotheses are not mutually exclusive as both take into account the shifts in conditions and prospects that affect women nearing menopause, which means the end of their reproductive career [60, 61]. The shifts in conditions that would enable twinning near the menopause relate to women's capacities, status, and context. During harsh ancestral times, women who were able to reach higher age probably successfully foraged, fought enemies, predators, parasites and disease, managed social alliances, acquired mate(s) and status, and survived the dangers of early childbirths [63–65]. This shows that women of a higher age in ancestral environments have stood the test of the time and, thus, had relatively better health and higher physical endurance, and social integration needed to successfully cope with multiple pregnancies. Moreover, older women would already have growing offspring that could act as 'helpers at the nest', alleviating part of the burden of twin childcare [66, 67]. The shifts in prospects that would enable twinning near the menopause related to the last chance for having own offspring, so having two or more babies at the same pregnancy would optimize and compensate for the later years without the possibility of new gestations.

However, considering the aforementioned risks of having a twin pregnancy, the pregnancies of mothers of higher age (≥35 years old), in general, are already associated with more chromosomal disease, complications, prematurity and low birth weight, and risks for abortion [68]. Thus, the fitness benefits of having twins in higher age must outweigh not only the costs of twinning, but also the costs of later age at conception.

1.3. Aim

In this chapter, we explore the general hypothesis that twinning represents an evolved physiological mechanism, particularly in mothers of higher age, as an 'all or nothing' last chance strategy for reproduction before menopause. We investigate twinning rates in representative data from São Paulo and the entire country of Brazil, and its distribution by age of the mother. We present decade-long, large-scale population data about maternities from the city of São Paulo and the entire country of Brazil. Moreover, by comparing the rates of dizygotic and monozygotic twinning among mothers of higher age in a São Paulo sample, we test both aforementioned hypotheses: the insurance ova hypothesis and the relaxed-screening hypothesis. If only dizygotic twinning rates increase maternal age, the insurance ova hypothesis would receive the most support. Alternatively, if both dizygotic and monozygotic twinning rates increase by the same amount with maternal age, the relaxed-screening hypothesis would receive the most support. Finally, if both dizygotic and monozygotic twinning rates increase

with maternal age, but dizygotic twinning increases more than monozygotic twinning, then both hypotheses would receive support. However, both of these theories focus mostly on DZ twinning, which has a very different origin than MZ twinning. Therefore, while the MZ results may be consistent with what the theories predict, a causal interpretation in terms of their origin may not be warranted.

2. Twinning rates in São Paulo city

The USP Twin Panel (*Painel USP de Gêmeos*), based in the Institute of Psychology—University of Sao Paulo since 2015, has investigated the live birth twinning rate from São Paulo city (Brazil) using public data and additional information during the years 2003–2014 [22]. The public data on the singleton, twin, and higher order multiple live-born births were drawn from the Health Department database of Live Births Information System of São Paulo (SINASC) and included all deliveries registered between the years 2003 and 2014, from all 140 hospitals (56 public and 84 private) of the 31 districts of the city. We contacted SINASC and upon agreement from the Human Research Ethics Committee at the Institute of Psychology, University of São Paulo (Protocol Number 1,418,827), we received a more detailed database that included infants' sex, identification of the mother, date and hour of the delivery, place of the delivery, and register number. Based on these refined data, we determined the sex composition of twin maternities using Weinberg's differential method, which is a populational equation based on the sex ratio and the proportion of same-sex and opposite-sex twins. The validity of Weinberg's rule has been debated over the years. Using large samples and applying statistical assumptions may improve its utility; see [39]. As standard in the literature, we computed maternity rates per 1,000 (‰): individual twin births were divided by two and individual higher order multiple births were divided by three, assuming that the far majority of higher order multiple births were triplets. Mothers' age was recoded into eight classes (<15, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44 and >45 years) (for details see, [22]).

For the first time in Brazil, we could establish live-birth rates in a decade-long, large-scale population sample encompassing 24,589 twin deliveries and 736 multiple deliveries out of a total of 2,056,016 deliveries during the studied time period. Precisely, the average rate of twin deliveries was 11.96‰, while the average of singletons was 987.42‰ and multiple births was 0.36‰. This was the largest study so far to calculate twinning rates in Brazil, which is in general in agreement with results from other countries [69], for example, Spain [70].

Interestingly, we found a strong positive correlation between the period (2003–2014) and twinning rate percentage and a strong negative correlation between the time period and both singleton rates and higher order multiple rates. This shows that while singletons and higher order multiple rates are diminishing, twinning rates are increasing. The twin birth rate rose 30.8% from 2003 to 2014, increasing from 10.19 to 13.33‰ [22]. Many factors may lead to this increase, such as increasing body mass index in women, improvement of quality of life, increase in social support, postponement of pregnancies until higher ages, use of assisted reproduction technologies and an increase in air pollution [22]. The pattern obtained in São Paulo city is

aligned with the pattern in earlier decades in São Paulo [71] and with the worldwide increase in twinning rates (e.g., [42, 72, 73]), especially over the last several decades [68].

2.1. Twinning as a function of mothers' age in São Paulo

We documented a positive influence of mothers' age on twinning rates, in particular, women aged 25 years or more have more twins than younger women. The opposite pattern appeared to characterize the singleton mothers. Mothers' age was the strongest positive predictor, with the time period also positively, although weakly, predicting the twinning rates. Together, age of the mother and the time period explained 63% of the total variation. The model for higher order multiple rates was also significant, explaining 25% of the total variation, and mothers' age was its only positive predictor [22].

Furthermore, we used the Weinberg's differential method in order to estimate the average frequency of MZ and DZ twinning rates. We found that the average twinning rate for the whole period was 4.42‰ for MZ and 7.15‰ for DZ twins [22]. These rates were comparably increasing throughout the time period (2003–2014). The mothers' age positively and significantly correlated with both MZ and DZ birth rates. The model for DZ twinning rates was highly significant, explaining 61.3% of the total variation. Mothers' age was the strongest positive predictor, with the time period also positively, although weakly predicting the twinning rates. The model for MZ twinning rates was also significant, explaining 17.1% of the total variation. Mothers' age was the only positive predictor of the MZ twinning rates [22]. This general finding, regardless of the zygosity, agrees with the literature both in Brazil [56, 71] and in other countries [58].

We found that women aged 45 or more had almost three times more DZ twins than mothers aged between 40 and 44 years and seven times more DZ twins than women aged between 20 and 24 years [22] (see **Figure 3**). This finding agrees with the view that polyovulation is a major cause of twinning in older ages as predicted by the insurance ova hypothesis. Moreover, we found that women aged 45 or more had two times more MZ twins than mothers aged between 40 and 44 years, and women aged between 20 and 24 years. This increase in MZ twinning in older mothers was predicted by the relaxed-screening hypothesis. Both hypotheses and proposed mechanisms can, thus, explain higher rates of DZ twinning in older mothers. Thus, our data support both evolutionary hypotheses for higher twinning near menopause, but the specific reasons behind MZ and DZ twinning at older maternal ages most likely differ. Importantly, different countries around the world have already sparsely but consistently found that not only DZ but also to a smaller degree MZ twinning rates were higher in mothers closer to menopause, in the U.S.A. population [74], in a Jewish population [75], in a Jewish and Bedouin populations [76], in rural and urban Chinese populations [77], and also in Spanish populations [70]. This cross-cultural convergence adds support to both evolutionary hypotheses, particularly to the relaxed-screening hypothesis [60, 61].

2.2. Variation in twinning rates in different city districts of São Paulo

Additionally, we closely investigated how twinning rates are distributed within various subregions of the city of São Paulo, the biggest metropolis of Brazil. Considering mothers' home
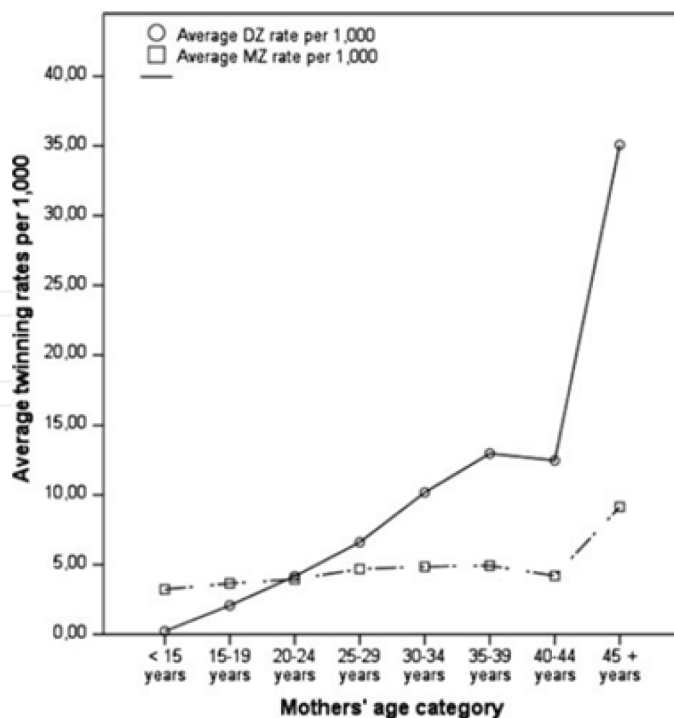
Figure 3. Dizygotic (DZ) and monozygotic (MZ) twin rates per 1,000 births as a function of mother's age; from [22].

addresses at the time of delivery, we found a large variance in the twinning rates among the 31 subregions of São Paulo: from 9.85 (district Itaim Paulista) to 24.32‰ (district Pinheiros). **Figure 4** shows the overall rate of twins' geographical distribution between 2003 and 2015 by the 31 subregions of the city. In **Figure 4**, we clearly show that in the central regions there are more twins born than in peripheral districts. This centralized distribution does not simply reflect the places where most hospitals are available, because we accessed the mothers' addresses and not the address of the maternity hospitals. Thus, this indicates that a real demographic factor is driving this distribution.

There was a pronounced positive correlation between the average income of each city district according to the 2010 Demographic census from Brazilian Institute of Geography and Statistics (IBGE) and the average twinning rates during the period from 2003 to 2015. The same result was found for the higher order multiple birth rates. This indicates that, in richer regions, there is a higher chance of twin and multiple births. This new finding from the USP Twin Panel can explain the centralized distribution of higher twinning rates shown in **Figure 4**. Many factors could be interacting to produce this result. Women with higher socioeconomic status tend to study longer and delay reproduction; thus, having offspring in higher age increases the chance of multiple pregnancies. Also those women can afford assisted reproduction technologies which increase the chance of multiple pregnancies. Moreover, those women have a richer and more diverse nutritional diet which, as found for nonhuman primates [1, 20], could increase the chance of multiple pregnancies. Colletto et al. [78] also found increased twinning rates as a function of women's higher socioeconomic
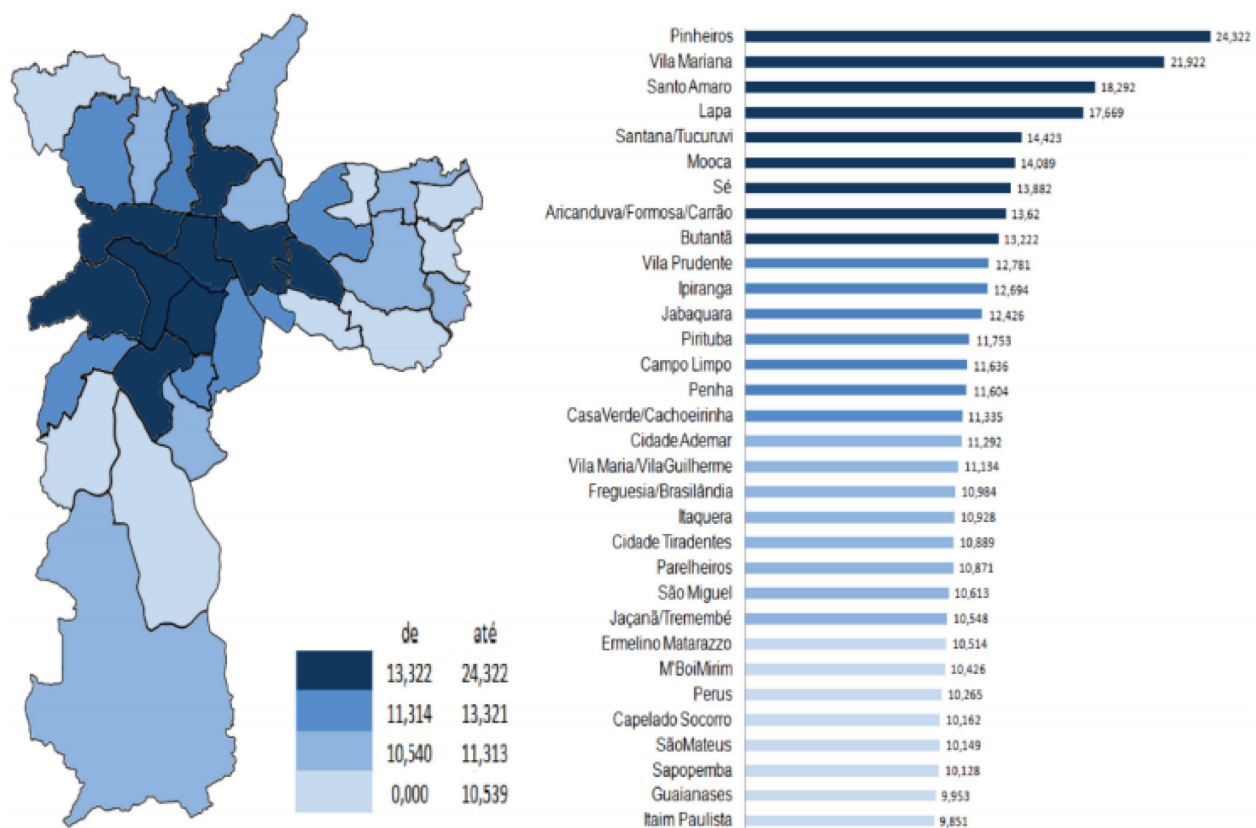
Figure 4. Overall geographical distribution of twinning rates between 2003 and 2015 by the 31 districts of the city. The darker the color, the higher the twinning rate. We used percentiles to create low, mid-low, mid-high, and high rates.

status. Further studies should attempt to disentangle the web of salient influential factors by accessing and integrating indicators such as nutrition, education, socioeconomic status, and assisted reproduction.

3. Twinning rates across the entire country of Brazil

Most recently, the USP Twin Panel (*Painel USP de Gêmeos*) has expanded the investigation of twinning rates to the entire country of Brazil between the years of 2002 and 2013. The data were drawn from TABNET within DATASUS, an official public governmental database and transformed into rates of maternities the same way it was done for the city of São Paulo [22]. A multivariate general linear model was used to explore the effects of region, maternal age, and time period on singleton, twin and higher order multiple birth rates. We obtained a total of 35,051,790 maternities between 2002 and 2013, 329,006 twinning maternities and 8,005 higher order maternities. Considering all regions of Brazil, the overall average rate of twins was 9.39‰ and higher order births were 0.23‰. These data show that the Brazilian countrywide twinning and multiple birth rates are lower than the twinning rates in the city

of São Paulo (11.96 and 0.36‰) [22]. These rates are slightly lower than results from developed countries (e.g., [69]). The increase in the twinning rate over the years was 14.54%, from 8.80‰ in 2002 to 10.08‰ in 2013, a modest increase compared to the 30.8% in São Paulo [22]. The decade time period positively predicted, albeit weakly, twin birth rates, explaining 3% of the variance. It also negatively predicted singleton rates, explaining 2% of the variance, with no effect on multiple birth rates.

3.1. Twinning as a function of mothers' age in the entire country of Brazil

Our results showed that maternal age strongly and positively predicted twin and multiple birth rates, explaining 56 and 21% of the variances, respectively. It also negatively predicted singleton birth rates, explaining 62% of the variance. These results are in agreement with the results from São Paulo [22, 56, 71] and from other countries, such as Spain [70].

The finding that the higher maternal age predicts twin and multiple births corroborates the evolutionary hypotheses, the insurance ova hypothesis [57, 59] and the relaxed-screening hypothesis [60, 61], pointing to the existence of an age-dependent mechanism that leads to a strong increase in twinning and multiple births in women near menopause.

3.2. Variation in twinning rates in different regions of Brazil

Among the five major regions of Brazil (North, Northeast, Central-West, South, and Southeast), we found a small, but significant variation in twinning rates. **Table 1** presents maternity rates for singletons, twins, and higher order multiple births divided by Brazilian regions. In general, the developed areas (e.g., Southeast) presented higher twinning and multiple birth rates than developing ones (e.g., North). This is in line with the finding of the São Paulo city districts. Similarly to the possible effects of higher maternal age, higher access to assisted reproduction technologies, and higher nutritional diversity and abundance may contribute to the higher twinning rates in the Southeast and South developed regions, yielding regional discrepancy.

Furthermore, the ethnic composition may also play a role. In the North of Brazil, there is the highest proportion of indigenous intermixed individuals within the population (up to 32%), while in other regions it ranges from 11 to 16% [79]. Brazilian native Americans are closely

Mean	Singleton rates (‰)	Twins rates (‰)	Higher order rates (‰)
Southeast	988.08	10.34	0.25
South	989.32	10.06	0.23
Central-West	990.70	9.05	0.24
Northeast	988.54	8.68	0.23
North	991.30	7.32	0.14

Table 1. Maternity rates of singleton, twin and higher order births per Brazilian regions.

related to Asiatic populations [80] that have the lowest twin rates compared to other ethnicities [39, 81]. It is thus possible that Asian ancestry may underlie the relatively lower twinning rate in the northern region of Brazil. Future studies should further explore the influencing factors among the regions.

4. Conclusions

The overall observed pattern of results linking increased twinning in mothers near menopause, from both decade-long large-scale populational studies, is consistent across São Paulo and all of Brazil, and agrees with the literature from Brazil [56, 71] and from other countries, for example, the Netherlands [58], and even with reports from traditional societies with natural reproduction, such as agricultural areas of Costa Rica [72], Gambia [55], eighteenth century Sweden [42], and seventeenth to eighteenth century French Canadian immigrants [41]. This convergence of results supports both evolutionary hypotheses about twinning: it points to the existence of an age-dependent evolved mechanism of twinning as an 'all-or-nothing' last chance strategy for reproduction near menopause. The estimated twinning rate per zygosity allowed us to closely test both the insurance ova hypothesis and the relaxed-screening hypothesis. In at least seven different populations worldwide [22, 70, 74–77], both DZ and MZ twinning rates increased in mothers near menopause; thus, both evolutionary theories received support, because it identifies polyovulation and relaxed screening as possible underlying mechanisms of increased twin births in women of higher age. The appreciation that also MZ twin births cross-culturally increases with mothers' age is an underappreciated pattern in the literature. Again, as stated earlier, these results require additional examination with respect to MZ twinning which has its origins explained by biological events that do not apply to DZ twinning (e.g., zygotic division).

Additionally, our results showed that higher socioeconomic conditions are related to higher twinning rates. This was found in both São Paulo and the entire country of Brazil, and corroborates the literature that has already shown a link between higher socioeconomic status and increased twinning rates in Brazil [78, 82] and other countries, for example, in Greece [83]. This finding also agrees with the literature on nonhuman primates that shows relatively higher twinning in captive, safer, and abundant conditions [1] and in species with more diverse nutritional intake [20].

This chapter reflects the importance of integrating factors and patterns from studies conducted on nonhuman species, particularly primates, with the findings traditionally focused on humans. We have attempted the first step toward bringing the comparative approach into light in order to promote deeper understanding of demographic data on twinning and higher order maternities. The comparative approach can offer insights and increase our understanding of both commonalities and specificities of the human case. Along the same lines, we have stressed the importance of considering proximate factors, such as genetic, physiological, ontogenetic and contextual variables, and distal factors, such as ancestral selective pressures, and evolutionary reasoning. Both fields have a great deal to gain with a more integrated approach.

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Conflict of interest

We authors declare no conflict of interest in preparing this chapter.

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