Mapping the past, present and future research landscape of paternal effects

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Abstract

Background: Although in all sexually reproducing organisms an individual has a mother and a father, non-genetic inheritance has been predominantly studied in mothers. Paternal effects have been far less frequently studied, until recently. In the last 5 years, research on environmentally induced paternal effects has grown rapidly in the number of publications and diversity of topics. Here, we provide an overview of this field using synthesis of evidence (systematic map) and influence (bibliometric analyses).

Results: We find that motivations for studies into paternal effects are diverse. For example, from the ecological and evolutionary perspective, paternal effects are of interest as facilitators of response to environmental change and mediators of extended heredity. Medical researchers track how paternal pre-fertilization exposures to factors, such as diet or trauma, influence offspring health. Toxicologists look at the effects of toxins. We compare how these three research guilds design experiments in relation to objects of their studies: fathers, mothers and offspring. We highlight examples of research gaps, which, in turn, lead to future avenues of research.

Conclusions: The literature on paternal effects is large and disparate. Our study helps in fostering connections between areas of knowledge that develop in parallel, but which could benefit from the lateral transfer of concepts and methods.

Keywords: Research weaving, Systematic review, Meta-analysis, Parental effects, Transgenerational effects, Transgenerational plasticity

Background

What does ocean acidification have in common with the Dutch famine? They both exert effects that can be non-genetically transmitted from the fathers to their offspring. Publications on such paternal effects (for definitions and nuances, see Table 1) are increasing in number and diversity, with research coming from evolutionary biology [22, 23], medicine [5, 11, 24] and toxicology [25]. Research on paternal effects carried out within those disciplines pursues different goals. For example, evolutionary ecologists seek to understand how paternal effects contribute to heritable variation, how they are influenced by the ambient environment and what role they play in evolution. By contrast, medical and health researchers seek to understand how male health and lifestyle can influence the health of descendants. In each of these disciplines, research is carried out using somewhat different tools and approaches. Cross-fertilization between these disciplines could be very valuable but has been hampered by the use of distinct terminologies and publication outlets.

While several thorough and influential reviews of paternal effect research have been published (e.g. [6, 25]), they are focused on a specific type of manipulation eliciting the non-genetic inheritance, or the proximate mechanisms mediating the phenomenon, rarely covering the entire field of paternal effects research. Meta-research (i.e. research on

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d) Interface of epigenetics and genetics

Evolutionary biologists delineate paternal effects most broadly [3]. In this field, a paternal effect reflects the influence of paternal environment or age on offspring traits and can be mediated by paternal care or by factors (such as RNA or proteins) in sperm of seminal fluid. The medical definition usually does not encompass effects transmitted via paternal care [4]. Researchers interested in inheritance of metabolic diseases narrow the definition further into ‘epigenetic programming’ [5] and do not consider age as a part of paternal effects. In terms of the proximate mechanisms, the definitions encompass sperm-borne mechanisms, such as DNA methylation, chromatin alterations and non-coding RNAs [3–6]. In addition, evolutionary perspective is likely to consider mechanisms acting via ejaculate-borne agents, e.g. RNA and proteins, reviewed by [7].

b) Meaning of paternal effect across the research fields

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c) The term ‘paternal effect’ in other contexts

Identity: the term is sometimes used to account for paternal identity in statistical models, either in a full-factorial experiment [8] or in studies designed to estimate genetic parameters of sires in animal breeding [9].

Genetics: the term could mean an effect that arises due to the male-specific sex chromosome [10]. The term can denote inheritance of genes through the paternal line which exhibits parent-of-origin expression [4], called also ‘epivariation’ [11]. ‘Paternal effect locus’ is a locus whose expression in a male influences the development of his offspring (i.e. an IGE). Recently, it is also referred to as ‘male genetic quality’, related to inbreeding [12].

Symbionts/parasites: although not commonplace, there is evidence that males may transmit symbionts [13] and parasites to their offspring. For instance, males with Wolbachia cause embryonic lethality [14]. There is also evidence for paternal mitochondria leakage in animals and humans [15]; these phenomena would be classified as male-specific genetic inheritance, yet to our knowledge have so far not been named ‘paternal effect’.

Assisted reproduction: in assisted reproduction treatment, the term ‘early paternal effect’ refers to failure at the initial stages of the procedure, resulting in zygote malformation, while ‘late paternal effect’ refers to the failure at the stage of implantation [16].

d) Interface of epigenetics and genetics

Research into paternal effects sheds light on interrelations between different forms of inheritance and their interactions with the environment. First, epigenotype controls the expression of the genotype, while both the genotype and the environment shape the epigenotype [17]. Second, environmentally induced epigenetic processes can promote genetic mutations [18]. Third, factors with mutagenic or cancerogenic effects can also exert epigenetic effects. Exposure to such factors (e.g. smoking) does not allow disentangling the epigenetic effect per se. Finally, classification of effects due to male age is ambiguous. Older males might accumulate effects of lifetime exposure to various environmental [19] and other factors (e.g. exercise). However, older males also have higher numbers of de novo mutations in germline DNA (reviewed, e.g. by [20]) and altered DNA methylation patterns, known as ‘epigenetic clock’ [21], which places age at the interface of genetic and non-genetic factors.
investigating trans-generational effects of diet and of psychological factors (Fig. 2a). The growth of empirical evidence is accompanied by the parallel growth of non-empirical papers (Fig. 2b), mostly narrative reviews, with notable scarcity of theoretical papers and systematic reviews (and derivatives [40]). From the secondary literature, we can conclude that the most attention in the field is currently directed towards common health outcomes of paternal exposures: metabolic disorders and detrimental effects of drugs and toxins. Existing reviews often present relatively narrow focus perspective: (1) researchers consider proximate mechanisms of paternal effects to a specific type of exposure, or (2) they associate specific exposure with particular offspring outcomes (Fig. 2c).

Three guilds in the paternal effect literature
As bibliometric clustering algorithm indicated, empirical research in the field of paternal effects has been carried out by three separate guilds, which we call toxicologists, medical scientists and ecology and evolution (eco-evo) researchers (Fig. 3a). Toxicologists maintain the most distinct research guild (Fig. 3b). They typically describe the effects of environmental factors that have negative effects both on the paternal and offspring generations. In this research cluster, there is a substantial share of observational (with a matched control group) studies on humans, while rodents are used as model species in experimental studies (Fig. 4a). We have found that this cluster is the oldest among the three (see Additional File: Fig. S1) and that
Fig. 2 Temporal trends in the map. a Timeline of numbers of published empirical papers split by different categories of paternal exposures (the same colour scheme is maintained in Fig. 4). b Timeline of numbers of published non-empirical papers split by type of publication. Among non-empirical records, ca. 80% are written as narrative reviews, followed by a smaller number of commentary/perspective works. Very few papers belong to systematic review family, and they are all from a medical cluster (e.g. [32–34]). Theoretical papers, presenting formal models, are even less frequent. The existing ones usually take evolutionary and/or ecological perspective [35–38], with the exception of one focused on the mechanisms of transgenerational inheritance of paternal stress [39]. c Primary (inner circle) and secondary (outer circle) topics of non-empirical studies broken down according to major taxonomic groups of considered organisms.
 individual publications are poorly connected even within the cluster (Fig. 3b).

The largest cluster belongs to medical scientists. In principle, we would expect that their studies are similar to those of toxicologists, because paternal exposures are also associated with negative effects on human health. However, a much broader scope of medical research makes their studies markedly different. Rodent studies dominate this cluster with relatively few studies on humans and other taxa (Fig. 4a). Medical scientists differ from toxicologists in their higher propensity for experimental, rather than observational, work. The medical cluster is the youngest and has the highest growth rate (Fig. S1).

The third cluster represents the work of eco-evo researchers. They differ from the other two research groups in also considering paternal effects that might be adaptive for the offspring. Eco-evo researchers have studied various taxonomic groups, including plants, arthropods and other invertebrates, fish, birds and, occasionally, rodents, but they have not studied humans, at least in our map (Fig. 4a). Eco-evo researchers frequently work with organisms in the wild or bring wild animals into captivity (Fig. 4a). The eco-evo cluster has an intermediate temporal distribution and rate of growth of publications (Fig. S1).

**Influence of and interest in paternal effect research**

Analyses of bibliometric influence (expressed as the number of citations per paper, Fig. 3c) show that, in each cluster, there are highly influential studies, both empirical and non-empirical. To exemplify where the attention of the research field is directed, we consider the three papers, ones with the highest number of citations in each cluster (Fig. 3d). Two of those papers present empirical work: one examines the inheritance of metabolic syndrome [42], while the other study examines how dioxin exposure affects offspring sex ratio [43]. The third highly influential paper is a classic review written from the evolutionary perspective [23]. Surprisingly, no articles in our map cite the paper by Ng and colleagues [42], which has the highest total number of citations (mostly by articles belonging to the subject area of “biochemistry, genetics and molecular biology”, as categorized by Scopus). The paper [42] demonstrates that paternal high-fat diet consumption leads to the intergenerational transmission of impaired glucose-insulin homeostasis. As such, it would be relevant for researchers studying dietary effects in eco-evo context and those investigating toxicants that alter glucose-insulin homeostasis.

**Landscape of experimental approaches**

Experiments on paternal effects pose substantial challenges and complexities. Such experiments should include three parties (fathers, mothers and offspring) in two states (experiment and control), resulting in up to six groups. Notable differences to the most basic experimental design, which involves only one party of subjects divided into experimental and control groups, are two-fold. First, researchers apply a treatment to one party of subjects (fathers), but they measure outcomes in different parties (offspring). Second, experiments addressing paternal effects require extra players (mothers), although the researchers usually pay little attention to this extra group. These complications have shaped the current experimental landscape in the paternal effect literature. In this section, we take a tour of this landscape (Fig. 4) through the lens of the three guilds of scientists which we identified in the last section and by following the three ‘main characters’ of the family story: father, mother and offspring.

**Father**

Obviously, fathers (or males) are the heroes of this experimental land. In the description of clusters, we have already uncovered who they are and where they are from. Here, we explore what kinds of challenges (exposures) they experience, and how they experience them.

**Types of paternal exposure**

Eco-evo researchers have a long tradition of studying the paternal effects of diet (Fig. 4a). Also, medical researchers have become increasingly interested in the transgenerational inheritance of the metabolic syndrome due to diet. Naturally, toxicologists have assessed chemical exposure (e.g. pesticides and solvents), mainly in humans, while ecologists measure effects of chemicals (environmental pollutants) on wildlife and non-model species. Somewhat surprisingly, toxicologists have studied the inter/trans-generational effects of medical drugs more than medical scientists. Yet, medical scientists seem to be the only group looking into the effect of paternal alcohol exposure. Both medical researchers and eco-evo researchers have shared their interest in studying (1) physiological exposures via experimental infection and (2) psychological exposures including various social (e.g. isolation or crowding) and physical (e.g. restraint, scent of predator) stressors. Finally, all types of scientists have studied paternal effects in relation to some abiotic aspects, such as water salinity, ambient temperature, electromagnetic field and light exposure.

**Interactions, dosage and timing of paternal exposures**

Most of the time, in a given study, fathers are exposed to only one challenge (94% of all studies). Yet, some researchers in each of the three fields have examined the effects of interaction of different categories of factors...
Fig. 3 (See legend on next page.)
acting on the father (for interacting effects between dietary components, see below). For instance, medical researchers have shown that paternal exercise alleviates the negative effect of obesogenic diet in mice [44, 45]. Eco-evo researchers have uncovered complex interactions between paternal age and immune challenge in insects [46].

It is more common to study dose-related responses to a single factor than interactions (approx. 20% of all studies). Toxicologists have always conducted dose-dependency studies [47]. Medical researchers also differentiate dosage in their studies of the effects of paternal alcohol exposure [48, 49]. Similarly, to reveal the effects of paternal age, researchers compare several groups of males of different age [50]. Eco-evo researchers have used gradients of exposures in plant studies [51]. They have also implemented nutritional geometry experiments in animal studies [52, 53], which allow them to reveal non-linear and fine-scale interactive effects of different dietary compounds.

Majority of studies (92% in toxicological, 79% in medical, 66% in eco-evo clusters) manipulate fathers at the adult stage, usually by subjecting them to exposure for one or two cycles of spermatogenesis. Researchers typically use patterns of exposure which mimic what fathers may encounter in real life (e.g. a heat wave [54]). Nonetheless, researchers could quantify those effects by combining exposure between weekdays and weekend [56]). Notably, some researchers have manipulated the time passed between exposure and mating. In case of medical drugs, this experimental design allows comparing acute and persistent effects of the exposure [57]. Further, such a design has shown that exposing fathers to chronic stress either at puberty or at adulthood had similar effects on offspring stress axis regulation [58].

Mother
As in old fairytales, this heroine has been a rather passive participant in the story. However, she has much to offer and can become a true heroine, as in newer stories. We believe that exciting unexplored possibilities exist when both the hero and the heroine face a challenge (exposure) together.

Mate choice and differential allocation The female can mediate the effects of male experiences in two potential, interrelated ways, one direct and one indirect. Her assessment of male quality can directly affect her prenatal and postnatal maternal investment in offspring [59]. Similarly, yet more indirectly, females could invest in offspring differentially if males induce such response via substances in their ejaculates [3, 4]. Both of these phenomena—via female perception and male substances—are referred to as maternal ‘differential allocation’ and have gained much attention, especially in evolutionary literature [60]. Although female differential allocation is interesting in its own right, to understand the magnitude, function and mechanism of paternal effects, we should limit the opportunity for maternally mediated effects.

Indeed, 77% of researchers across the field have blocked female mate choice by paring up a single male and female (with the exception of human studies). In addition, the researchers predominantly use virgin females (but see [56]). While these two approaches reduce maternal effects due to female perception of male quality, they cannot eliminate them. Eco-evo researchers are most likely to control for differential allocation due to female perception (30%), usually by capitalizing on species with external fertilization [61] or by the means of artificial fertilization in plants, fish and birds [62]. Researchers in medicine control for maternal effects rarely (12%), yet using the greatest variety of methods, including in vitro fertilization [63], embryo transfer [64] and offspring cross-fostering [65]. Toxicologists have rarely dealt with this issue (5%).

Differential allocation induced by male substances is even more challenging to control for, and therefore, only a few have done so to date (e.g. [66]). Nonetheless, researchers could quantify those effects by combining artificial insemination with the use of vasectomized males, which allows assessing the effects of seminal fluid substances. Medical researchers have carried out such studies occasionally [67]. In a similar vein, eco-evo researches have used the so-called telegony approach. Under this approach, a female is mated with two males, both of whom contribute to her offspring phenotypes: the one as a genetic father and the other via semen-mediated effects (only two studies in our collection used this approach [68, 69], see also [70]).

Maternal exposure: comparison and synergy Researchers can expose mothers to the same challenges as fathers (Fig. 4b). Such a venture opens up possibilities of answering additional questions, but a careful experimental
Fig. 4 (See legend on next page.)
design is warranted. Toxicologists commonly use a design comparing two groups of offspring from biparental exposure vs. non-exposure groups (e.g. [71]). Unfortunately, such a simplistic design precludes assessment of paternal (or maternal) effect alone; accordingly, these studies are not included in our map. Assessing the relative strength of paternal compared to maternal effects is possible when we expose fathers and mothers independently and then pair them up with control individuals (see also Fig. 5f). Sometimes, it is inevitable that exposed partners reproduce only with control (e.g. human medical studies [72, 73]), precluding analyses of the effect of combined exposure.

The most informative is a two-by-two factorial design (also known as North Carolina II). This design enables not only comparing the effect of each parent separately, but also estimating the synergistic (interactive) effect of both [74]. Using the factorial design (55%, Fig. 4b), many of eco-evo researchers have found that the father and mother can have a synergistic effect on offspring (e.g. [75]), but their effects could also cancel each other (e.g. [76]).

**Offspring**

Finally, we turn to the children, who are an essential part of the story, but often neglected. Scientists take many different measurements from the children (offspring) at different times, but they often forget that we have both princes and princesses. Moreover, we find some scientists have also challenged the children, enriching the story plot, while others failed to do so.

**Measurements: timing, sex-specific and multigenerational effects** Toxicologists, more than others, confine their studies to effects on offspring development; only 30% of their studies track offspring to adulthood. Many medical scientists, in contrast, investigate offspring performance up to adulthood (i.e. 70%, facilitated by the use of relatively fast-maturing lab rodents). Eco-evo researchers also often monitor offspring through development until adulthood (62%), although their monitoring could stop at the juvenile (or larval) stage. Therefore, data on offspring phenotype in the three clusters complement each other, highlighting possibilities of knowledge transfer across the disciplines in this respect.

Researchers who cease the study at early stages of offspring development usually lack information on offspring sex. Although toxicologists have been interested in whether paternal exposure affects sex ratio [77], surprisingly, they are also the least likely to account for offspring sex (34%) in assessing offspring traits. In contrast, medical scientists are the keenest to report effects for the two sexes separately, but also to study only one sex (65% for those two approaches combined). Given the interest in parent-of-origin epigenetic inheritance (Table 1), researchers should routinely examine sex specificity of paternal effects in the offspring [78, 79]. Unfortunately, this is not the case. Instead, the large body of existing literature (63%) has not taken opportunities to detect such sex-specific patterns.

Our map has shown that only ca. 10% of studies examined the transfer of paternal effects to the grand-offspring generation or beyond. Yet, a multigenerational study can provide insights into the nature and persistence of paternal effects. The medical cluster has included such multigenerational studies: the consequences of F0 generation exposure to high-fat diet [80] and heroin addiction [81], in both of which paternal effects were followed up to F3 generation descendants.

**Offspring exposure: matching, mismatching and beyond**

As mentioned earlier, medical scientists and toxicologists have focused on the negative effects of paternal exposures. Thus, it may not be surprising that toxicologists never expose offspring to the same damaging factors (chemicals and drugs, Fig. 4b), although medical scientists have sometimes done so (12%). In contrast, nearly half (47%) of the eco-evo researchers expose offspring to the same factor as fathers. They compare offspring under matched and mismatched conditions to those experienced by their fathers to see if fathers prepare offspring for the same environment via so-called anticipatory paternal effects (sensu [82, 83]). However, to properly investigate anticipatory paternal effects, the experimental design should be based on environmental predictability over the space and time [84]. A proper study should include evidence of the likelihood that the offspring generation will face the same environment as their fathers [84]. In practice, we are aware of no such studies.

**Gaps and opportunities: three examples**

We have highlighted what researchers have done so far. Yet, systematic mapping can also elucidate knowledge gaps in the research field [29]. Here, among many potential gaps,
Empirical research approaches:

- design / clarity

a. 
- measuring traits relevant for paternal exposure
- exposing offspring to the same factor as fathers
- measuring offspring fitness
- providing cues on the expected offspring environment

b. 
- relative strength of paternal versus maternal effects and their interaction
  - within-group mating
    - E E C C
    - C E E C
  - only paternal exposure
    - C E E C
  - independent maternal exposure
    - C E E C
  - North Carolina II design
    - C E E C

c. 
- maternal-mediated effects via the female perception
  - assessment of female preferences
  - assessment of maternal behavior
  - offspring cross-fostering or embryo transfer
  - in vitro fertilization or artificial insemination
  - external fertilization

- mechanisms

- proximate
- ultimate

d. 
- maternal differential allocation via opportunity for mate choice
  - no mate choice
    - ♀ + ♂
  - additional experimental group
    - ♀ + ♂ ♂
  - mate choice
    - ♀ + ♂ ♂ ♂
    - quantifying the consequences of a given mating setup

e. 
- maternal-mediated effects via male semen-borne substances
  - vasectomized males
  - telegony
  - external fertilization / in vitro

f. 
- male relatedness/pedigree
  - inbred males
  - paired-sample design
  - systematically heterogenized sample
  - reduced unexplained variation
  - generalizable results

Fig. 5 (See legend on next page.)
we choose to discuss three examples and show how we can turn these gaps into future research opportunities.

**Oversight over paternal effects in livestock?**

Our map, somewhat surprisingly, revealed that paternal effects are neglected in the field of animal breeding (Fig. 4a). In the livestock industry, the choice of sire that produces hundreds of offspring is of paramount importance, and thus, the sire should be of prime quality. Selection schemes of sires usually employ quantitative genetic tools. Thus, much of heritability (due to genetics) is accounted for. However, simultaneous accounting for the epigenome should improve the accuracy of prediction of breeding values. Indeed, among researchers studying farm animals/livestock breeding, there is already an interest in non-genetic paternal inheritance due to sex-specific gene expression patterns [85]; see also Table 1. In terms of environmentally induced paternal effects, it remains unknown what treatment to impose on fathers and which traits to measure in their offspring [17, 86, 87]. Our map could inspire potential research pathways in this field. For example, one of the promising directions would be to manipulate the variability of paternal exposure and, optimally, expose some offspring to the same factor as the father. If possible, study offspring fitness traits. For the best outcomes, include cues that allow prediction of the offspring environment by the fathers. To measure the relative strength of paternal vs. maternal effects, expose female to the same factor as male. Do not mate the parents only within the experimental group (red indicates the design to be avoided). Pair-up exposed parents with control partners to compare maternal and paternal effects. Use North Carolina II design to assess the synergistic effects of both parents. To estimate maternal-mediated effects due to females’ perception, assess female preference for the male and/or maternal behaviour in relation to paternal treatment. Use embryo transfer and offspring cross-fostering. To eliminate effects due to female perception, use in vitro fertilization and artificial insemination. Study species with external fertilization. Allow mate choice, if interested in ultimate aspects of paternal effects. Reduce mate choice, if searching for proximate mechanisms. Add experimental groups to understand the consequences of a particular mating set-up. To reduce maternal-mediated effects due to male semen-borne substances, use vasectomized males, helping identify the proximate mechanism of paternal effects. One could also use telegony approach. To separate female-mediated effects (via male substances and female perception), use species with external fertilization. Use highly related males to reduce unexplained variation and facilitate identification of proximate mechanisms of paternal effects. To obtain robust results, use heterogeneous, randomized sample of males. Using males in a paired-sample design could often be a convenient and powerful option.

**In search of paternal bet-hedging**

In the face of a stressful and unpredictable environment, mothers should increase variance in offspring traits by employing a so-called bet-hedging strategy [96]. Environmentally stressed fathers should use a similar strategy, as long as the fitness benefits to the male outweigh the costs of investing in such a strategy. Yet, although maternal bet-hedging has been a popular research topic, and the outcomes of the existing studies are mixed [96], we are not aware of any studies examining bet-hedging (via non-genetic effects) by fathers. This gap could be addressed in a number of ways. In terms of empirical studies, the most intuitive approach would be to manipulate the variability of paternal environment and analyse the difference in variance in offspring between treatment groups (i.e. test for heteroscedasticity [97]). Such a study should differentiate between an adaptive male strategy of producing offspring with increased phenotypic variance and a non-adaptive effect of stressful environment on male reproductive physiology. A meta-analytical approach to study paternal bet-hedging is also possible [98], providing that paternal exposures can be
unambiguously classified as those that should promote increased or reduced variation in offspring traits. Finally, a recent theoretical model of genomic imprinting [99] predicts reduced variation in offspring phenotype due to paternally (compared to maternally) expressed genes, if males have higher reproductive variance. So far, there are no theoretical models predicting how environmentally induced non-genetic paternal effects affect variation in offspring traits. Thus, such a model is needed.

Improving paternal effect research for posterity

We have given you a guided tour of our map of the parental effect research through the lens of the three guilds of researchers, three family members and three examples of research gaps. Based on our journey, we offer six considerations for designing future experiments on paternal effects:

a) Assessing whether paternal effects benefit offspring health and fitness
b) Quantifying paternal, maternal and their interactive effects
c) Lessening or eliminating maternally mediated effects via female perception
d) Allowing opportunities for mate choice to study maternal differential allocation
e) Isolating or eliminating maternally mediated effects via male semen-borne substances
f) Considering male relatedness to reduce confounds or enhance generalisability

The first three considerations are useful for singling out paternal effects and clarifying their function, whereas the latter three are concerned with designs suitable for understanding proximate or ultimate mechanisms (Fig. 5). All the considerations provide options depending on researchers’ interest, their study organisms and other logistics. They also provide opportunities for cross-fertilizations of approaches and ideas from the three clusters of scientists. For example, medical researchers often employ sophisticated techniques to elucidate the proximate mechanisms mediating paternal effects [63, 64], and some of these techniques could be utilized by other researchers. Conversely, eco-evo researchers test predictions derived from theory [22, 23] and focus their experiments on ecologically relevant effects. Some of the insights gained from evolutionary and ecological theory could inform the design of medical and toxicological research [4]. Toxicologists typically investigate the effects of a range of treatment levels [47], and such an approach can facilitate the detection of subtle or non-linear effects of the paternal environment on offspring. Such inter-disciplinary links between the three clusters could enhance paternal effect research overall.

Conclusions

Research into paternal effects is multidisciplinary. However, currently, three relatively insular clusters exist in this research field. We call for more cross-disciplinary collaborations among the three guilds. Further, we note that the importance of paternal effects does not stop at the individual level and that paternally induced changes could propagate into the population and meta-population scales [100]. Altogether, we have much to hope for in the future of the paternal effect research. It will bridge disparate fields of research and will continue to provide useful insights into topics ranging from public health, environmental pollution and climate change to animal science. We can also expect much interest from members of the public by showing that there might be much more than genes to the saying ‘like father, like son’.

Methods

Systematic map

The map is based on the published papers on environmentally induced non-genetic paternal germline and semen effects (i.e. when the male had been exposed to some environmental factor before fertilization and the effects were studied in the offspring anytime from the fertilization onwards; Fig. 1a); importantly, it does not include the effects of paternal care, which role is well documented [101–103]. PECO (Population, Exposure, Comparators and Outcomes) statement is available in Additional File: Table S1.

Relevant records were identified via searches carried out in Scopus and Web of Science databases on 11 April 2019. Sets of keywords are summarized in Fig. 1b, see also Additional File for the exact search string.

The procedure applied after the literature search is presented in a PRISMA diagram [28] (Fig. 3c). In short, we uploaded unique records to Rayyan (https://rayyan.qcri.org/) to perform the initial screening based on the title, abstract and keywords. The screening was done independently by two researchers. We excluded records that did not fulfil all the criteria outlined in the PECO statement. We classified records that fulfilled the inclusion criteria as empirical or non-empirical. We used the Zotero reference manager (https://www.zotero.org/) to retrieve full texts of the designated records. One person coded full texts, with 42 cross-checked by the second person. We uploaded separate datasets of empirical (references [42–58, 61–65, 67–69, 72–77, 80, 81, 83, 88, 90, 91, 104–404]) and non-empirical (references [3–6, 11, 19, 20, 23–25, 32–39, 87, 103, 405–518]) layers into R v.3.6.0 [519] and visualized their content using ggplot2 package [520]. We analysed the combined datasets using the bibliometrix package [41] and VOSviewer (https://www.vosviewer.com/) [521]. Full details of the methods are provided in the Additional File.
Bibliometric analyses
We downloaded relevant bibliometric records from Scopus database on 16 July 2019. We ran bibliometric coupling analysis in VOSviewer [521] to find clusters in paternal effect literature (Fig. 3a). The unit of analysis was ‘document’ (i.e. each paper). We used a factorial counting method, which equalizes the weight given to each paper, regardless of whether it has been cited, and fractionalization method to visualize the outcome. Clustering resolution was set to 0.8 and minimal cluster size to 60. The resulting number of three clusters was a stable outcome when minimal cluster size parameter was varied between 51 and 79. We named the clusters based on their dominant research discipline, i.e. medical (Med), toxicological (Tox) and eco-evolutionary (EcoEvo).

We calculated the index of bibliographic connection between papers in the three clusters (Fig. 3b) following [522]. The index parameter reflects how many connections are there given the number of all possible connections that could exist between two different clusters and with the cluster itself. The mean connectivity index for our clusters is 0.16 due to low connectivity between clusters and also within clusters themselves. To put this index value into perspective, life-history theory literature, analysed using the same approach, was characterized by a mean index of 0.56 for studies published before 2010 and 0.35 for those published after 2010 [522]. Low connectivity indices may be linked to a rapid increase of volume of available research (although it is not a default relationship), but it may also indicate that literature relevant to a given topic goes unnoticed.

Supplementary Information
Supplementary information accompanies this paper at https://doi.org/10.1186/s12915-020-00892-3.

Additional file 1. 1. Additional results (Figure S1). Temporal distribution of records belonging to the three clusters. 2. Paternal effects PECO statement regarding empirical papers (Table S1). 3. Search string. 4. Decision trees for initial screening based on abstracts, titles and keywords (Figure S2, Figure S3). 5a. Additional information on selection criteria. 5b. Limitations of the map. 6a. Questionnaire 1, used in full-text coding for the purpose of the map of empirical records. 6b. Questionnaire 2, used in full-text coding for the purpose of the map of non-empirical records. 7. Amendments to the initial protocol. 8a. List of papers excluded based on full text with the reasons – non-empirical layer. 8b. List of papers excluded based on full text with the reasons – empirical layer.

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Authors’ contributions
JR conceived and led the designing of the study. JR and ML performed the initial trials leading to the choice of the search string and pilot rounds of abstract exclusion and full-text coding. JR carried out the full-text coding and analyses with input from ML and SN. JR and SN wrote the paper with input from ML and RB. All authors discussed the project and contributed to the final version. The authors read and approved the final manuscript.

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References
1. Mousseau TA, Fox CW. The adaptive significance of maternal effects. Trends Ecol Evol. 1998;13(10):403–7.
2. Wolf JB, Brodie III ED, Cheverud JM, Moore AJ, Wade ML. Evolutionary consequences of indirect genetic effects. Trends Ecol Evol. 1998;13(2):64–9.
3. Crean AJ, Bonduriansky R. What is a paternal effect? Trends Ecol Evol. 2014;29(10):554–9.
4. Curley JP, Marshoodh R, Champagne FA. Epigenetics and the origins of paternal effects. Horm Behav. 2011;59(3):306–14.
5. Hur SSJ, Cropley JE, Suter CM. Paternal epigenetic programming: evolving metabolic disease risk. J Mol Endocrinol. 2017;58(3):159–68.
6. Champroux A, Cocquet J, Henry-Berger J, Drevet JR, Kocer A. A decade of exploring the mammalian sperm epigenome: paternal epigenetic and transgenerational inheritance. Front Cell Dev Biol. 2018;650.
7. Crean AJ, Adler ML, Bonduriansky R. Seminal fluid and mate choice: new predictions. Trends Ecol Evol. 2016;31(4):253–5.
8. Núñez J, Castro D, Fernández C, Duguel R, Chu-Koo F, Duponchelle F, García C, Renno J-F. Hatching rate and larval growth variations in Pseudoplatystoma punctatum: paternal and maternal effects. Aquac Res. 2011;42(6):764–75.
9. Hamann H, Steinheuer R, Distl O. Estimation of genetic parameters for litter size as a sow and boar trait in German herdbook Landrace and Pietrain swine. Livest Prod Sci. 2004;85(2–3):201–7.
10. Friberg U, Stewart Andrew D, Rice William R. X- and Y-chromosome linked paternal effects on a life-history trait. Biol Lett. 2012;8(1):71.
11. Rando OJ. Daddy issues: paternal effects on phenotype. Cell. 2012;151(4):702–8.
12. Malo AF, Gilbert TC, Riordan P. Drivers of sex ratio bias in the eastern bongo: lower inbreeding increases the probability of being born male. Proc R Soc B Biol Sci. 2019;286(1902):20190345.
13. Damiani C, Ricci I, Cotti E, Rossi P, Rizzi A, Scuppa P, Esposito F, Bandi C, Daffonchio D, Favia G. Paternal transmission of symbiotic bacteria in malaria vectors. Curr Biol. 2008;18(23):R1087–8.
14. Liu C, Wang J-L, Zheng Y, Xiong E-J, Li J-J, Yuan L-L, Yu X-Q, Wang Y-F. Wolbachia-induced paternal defect in Drosophila is likely by interaction with the juvenile hormone pathway. Insect Biochem Mol Biol. 2014;49:49–58.
15. Luo S, Valencia CA, Zhang J, Lee N-C, Stone J, Gui B, Wang X, Li Z, Dell S, Brown J, et al. Biparental inheritance of mitochondrial DNA in humans. Proc Natl Acad Sci. 2018;115(51):E13093–44.
16. Mendoza C, Greco E, Tesark J, Late, but not early, paternal effect on human embryo development is related to sperm DNA fragmentation. Hum Reprod. 2004;19(3):611–5.
17. Gonzalez-Recio O, Toro M, Bach A, Past, present and future of epigenetics applied to livestock breeding. Front Genet. 2015;6:305.
18. Skinner MK. Environmental epigenetics and a unified theory of the molecular aspects of evolution: a neo-Lamarckian concept that facilitates neo-Darwinian evolution. Genome Biol Evol. 2015;7(5):1296–302.
41. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523–52.

26. Ioannidis JPA, Fanelli D, Dunne DD, Goodman SN. Meta-research: evaluation of research and meta-analyses. Hum Reprod Update. 2018;24(3):320–331.

21. Horvath S, Gurven M, Levine ME, Trumble BC, Kaplan H, Allayee H, Ritz BR, Janecka M, Mill J, Basson MA, Goriely A, Spiers H, Reichenberg A, Schalkwyk LC, Rutkowska et al. BMC Biology 2017;16(7):171–171.

20. Janecka M, Mill J, Basson MA, Goriely A, Spiers H, Reichenberg A, Schalkwyk LC, Rutkowska et al. BMC Biology 2017;16(7):171–171.

19. Mashoodh R, Champagne FA. Paternal epigenetic inheritance; 2014. p. 221–35.

18. Janecka M, Mill J, Basson MA, Goriely A, Spiers H, Reichenberg A, Schalkwyk LC, Rutkowska et al. BMC Biology 2017;16(7):171–171.

17. Galloway LF. Parental environmental effects on life history in the herbaceous plant Campanula americana. Ecology. 2001;82(10):2781–9.

16. Bonduriansky R, Runagall-McNaull A, Crean AJ. The nutritional geometry of paternal effects: maternal and paternal macronutrient consumption and offspring phenotype in a neriid fly. Funct Ecol. 2016;30(10):1675–86.

15. Polak M, Simmons LW, Benoit JB, Ruohonen K, Simpson SJ, Solon-Biet SM. Nutritional geometry of paternal effects on embryo mortality. Proc R Soc B Biol Sci. 2017;284(171492).

14. Zhu B, Walker SK, Oakey H, Setchell BP, Maddock S. Effect of paternal heat stress on the development in vitro of preimplantation embryos in the mouse. Andrologia. 2004;36(6):384–94.

13. Hao HH, Li JT, Zhao N, Zhang L, Fu Y, Zhang YJ, Chen RX, Zhang JM. Biobehavioral effects produced by paternal sleep disturbances. Sleep Biol Rhythms. 2015;13(3):235–41.

12. George VK, Li H, Teloken C, Grignon DJ, Lawrence WD, Dhabuwala CB. Effects of long-term cocaine exposure on spermato genesis and fertility in periuberal male rats. J Urol. 1996;155(1):327–31.

11. Favareto AP, de Toledo FC, Kempinas Wd G. Paternal treatment with cisplatin impairs reproduction of adult male offspring in rats. Reprod Toxicol. 2011;32(4):425–33.

10. Rodgers ASB, Morgan CP, Bronson SL, Revello S, Bale TL. Paternal stress exposure alters sperm microRNA content and reprograms offspring HPA stress axis regulation. J Neurosci. 2013;33(21):9003–12.

9. Sheldon BC. Differential allocation: tests, mechanisms and implications. Trends Ecol Evol. 2000;15(10):397–402.

8. Champagne FA. Interplay between paternal germline and maternal effects in shaping development: the overlooked importance of behavioural ecology. Funct Ecol. 2020;34(2):401–13.

7. Jensen N, Allen RM, Marshall DJ. Adaptive maternal and paternal effects: gamete plasticity in response to parental stress. Funct Ecol. 2014;28(3):724–33.

6. Li Y, Lei X, Guo W, Wu S, Duan Y, Yang X, Yang X. Transgenerational endotoxin tolerance-like effect caused by paternal dietary Astragalus polysaccharides in broilers’ jejunum. Int J Biol Macromol. 2018;111:769–79.

5. Chen Q, Yan MH, Cao ZH, Li X, Zhang YF, Shi JC, Feng GH, Peng HY, Zhang XD, Zhang Y, et al. Stem tRNAs contribute to intergenerational inheritance of an acquired metabolic disorder. Science. 2016;351(6271):397–400.

4. Mashoodh R, Habroylo JB, Gudnuk KM, Pelle G, Champagne FA. Maternal modulation of paternal effects on offspring development. Proc R Soc B Biol Sci. 2018;285(1841):2018118.

3. Dai JB, Wang ZX, Wu JW, Zhang MX, Zhu ZJ, Zhao XL, Zhang D, Nie DS, Wang LY, Qiao ZD. Paternal nicotine exposure defines different behavior in subsequent generation via hyper-methylation of mnu-mir-15b. Sci Rep. 2017;7(1):7286.

2. Simmons LW. Allocation of maternal- and ejaculate-derived proteins to subsequent generation via hyper-methylation of mnu-mir-15b. Sci Rep. 2017;7(1):7286.

1. Watkins AJ, Dais I, Tsuro H, Allen D, Emes RD, Moreton J, Wilson R, Ingram RJM, Sinclair KD. Paternal diet programs offspring health through sperm- and seminal plasma-specific pathways in mice. Proc Natl Acad Sci U S A. 2018;115(40):10064–9.
68. Crean AJ, Koppes AM, Bonduriansky R. Revisiting telegeny: offspring inherit an acquired characteristic of their mother’s previous mate. Ecol Lett. 2014;17(12):1545–52.

69. Eggert H, Kurtz J, Diddens-de Buhr MF. Different effects of paternal transgenerational immune priming on survival and immunity in step and genetic offspring. Proc R Soc B Biol Sci. 2014;281(142089).

70. Simmons LW, Lovegrove M. Nongenetic paternal effects via seminal fluid. Evol Lett. 2019;3(4):403–11.

71. Ganiger S, Malleshappa NN, Krishnappa H, Rajashankar G, Ramakrishna Rao V, Sullivan F. A two generation reproductive toxicity study with curcumin, turmeric yellow, in Wistar rats. Food Chem Toxicol. 2007;45(1):64–9.

72. Zuccolo L, DeRoo LA, Wills AK, Smith GD, Suren P, Roth C, Stoltenberg C, Magnus P. Pre-conception and prenatal alcohol exposure from mothers and fathers drinking and head circumference: results from the Norwegian Mother-Child Study (MoBa). Scand. Rep. 2016;36:9535.

73. Messorian C, Bellinger D, Minguez-Alarcón L, Romano ME, Ford JB, Williams PL, Calafat AM, Hauser R, Braun JM. Paternal and maternal preconception urinary phthalate metabolite concentrations and child behavior. Environ Res. 2017;158:720–8.

74. Fox CW, Waddell KJ, Mousaou TA. Parental host-plant affects offspring life-histories in a seed beetle. Ecology. 1995;76(2):402–11.

75. McNamara KB, Li L, Loechstedt E, Simmons LW. The effect of maternal and paternal immune challenge on offspring immunity and reproduction in a cricket. J Evol Biol. 2014;27(6):1000–8.

76. Zirbel KE, Alto BW. Maternal and paternal nutrition in a mosquito influences life histories but not infection with an arbovirus. Ecosphere. 2018;9(10):e02649.

77. Li JH, Jiang DP, Wang YF, Yan J, Guo QY, Miao X, Lang HY, Xu SL, Liu JY, Guo GZ. Influence of electromagnetic pulse on the offspring sex ratio of male BALB/c mice. Environ Toxicol Pharmacol. 2017;54:155–61.

78. Klein SL, Schiebinger L, Stefanick ML, Cahill L, Danska JS, de Vries GJ, Miao X, Lang HY, Xu SL, Liu JY, Guo QY. Influence of electromagnetic pulse on the offspring sex ratio of male BALB/c mice. Environ Toxicol Pharmacol. 2017;54:155–61.

79. Prendergast BJ, Onishi KG, Zucker I. Female mice liberated for inclusion development due to mating with immunised males. Reprod Fertil Dev. 2016;9(1):31.

80. Klussmann K, Naquiah MZF, James RJ, Suratman S, Lee LS, Hafidz MIM, Salleh MZ, Teh LK. The effects of maternal alcohol consumption on offspring intrauterine growth retardation, placental, and placenta–fetal weight ratio in the Rattus norvegicus. PLoS One. 2015;10(10):e0140195.

81. Masuyama H, Mitsui T, Eguchi T, Tamada S, Hiramatsu Y. The effects of maternal ethanol consumption on offspring behavioral development in rats. Alcohol. 1995;12(1):1–6.

82. Crean AJ, Marshall DJ. Coping with environmental uncertainty: dynamic bet hedging as a maternal effect. Philos Trans R Soc B Biol Sci. 2009;364(1520):1087–96.

83. Cleasby IR, Nakagawa S. Neglected biological patterns in the residuals: a behavioural ecologist’s guide to co-operating with heteroscedasticity. Behav Ecol Sociobiol. 2011;65(12):2361–72.

84. Nakagawa S, Poulin R, Mengersen K, Reinhold K, Engqvist L, Lagisz M, Senior AM. Meta-analysis of variation: ecological and evolutionary applications and beyond. Methods Ecol Evol. 2015;6(2):143–52.

85. Wilkins JF, Bhattacharya T. Infrageneric conflict over bet-hedging. Philos Trans R Soc B Biol Sci. 2019;374(1766):20180142.

86. Seidbacher F, Krause J. Epigenetics of social behaviour. Trends Ecol Evol. 2019;34(9):818–30.

87. Charpentier MJ, De Vries GJ, Stefanick ML, Cahill L, Danska J, Miao X, Lang HY, Xu SL, Liu JY, Guo QY. Influence of electromagnetic pulse on the offspring sex ratio of male BALB/c mice. Environ Toxicol Pharmacol. 2017;54:155–61.

88. Head ML, Berry LK, Royle NJ, Moore AJ. Paternal care: direct and indirect genetic effects of fathers on offspring performance. Evolution. 2012;66(11):3570–81.

89. Braun K, Champagne FA. Paternal influences on offspring development: behavioural and epigenetic pathways. J Neuroendocrinol. 2014;26(10):697–706.

90. Abel EL. Paternal alcohol consumption: effects of age of testing and duration of paternal drinking in mice. Teratology. 1989;40(5):467–74.

91. Abel EL. Rat offspring sired by males treated with alcohol. Alcohol. 1993;10(3):237–42.

92. Abel EL. Paternal alcohol exposure and hyperactivity in rat offspring: effects of amphetamine. Neurotox Res. 1993;15(6):445–9.

93. Abel EL. Effects of phystosmine on male offspring sired by alcohol-treated fathers. Alcohol Clin Exp Res. 1994;18(3):648–52.

94. Abel EL. A surprising effect of paternal alcohol treatment on rat fetuses. Alcohol. 1995;12(1):1–6.

95. Abel EL. Bilizlite P. Paternal alcohol exposure: paradoxical effect in mice and rats. Psychopharmacology. 1990;100(2):159–64.

96. Abel EL. Moore C. Effects of paternal alcohol consumption in mice. Alcohol Clin Exp Res. 1987;11(8):533–5.

97. Abel EL. Tan SE. Effects of paternal alcohol consumption on pregnancy outcome in rats. Neurotox Res. 1988;10(3):187–92.

98. Adler MI, Bonduriansky R. Paternal effects on offspring fitness reflect father size and social environment. Evol Biol. 2013;40(2):288–92.

99. Al-Juboori B, Hamdan F, Al-Salihi A. Paternal exposure to low-dose lead and aluminum in drinking water and high-fat diet during pregnancy affects offspring liver RNA expression and progeny development in rats. Toxicol Rep. 2015;2:23–41.

100. Seebacher F, Krause J. Epigenetics of social behaviour. Trends Ecol Evol. 2019;34(9):818–30.
121. Beemelmanns A, Roth O. Biparental immune priming in the pipefish Synagrus typhle. Zoology. 2016;119(4):262–72.
122. Beemelmanns A, Roth O. Grandparental immune priming in the pipefish Synagrus typhle. BMC Evol Biol. 2017;17(1):1–15.
123. Bellei AR. Incorporation of (3H)uridine by mouse embryos with abnormalities induced by parental hyperthermia. Biol Reprod. 1976;15(5):632–46.
124. Beltrame D, Di Salle E, Gavioli E, Gunnarsson K, Brugga M. Reproductive toxicity of exeremantine, an antinomual arnastatze, in rats and rabbits. Reprod Toxicol. 2001;15(2):195–213.
125. Berk RS, Montgomery RH, Hazlett ID, Abel EL. Paternal alcohol consumption: effects on oocyte response and serum antibody response to Pseudomonas aeruginosa infection in offspring. Alcohol Clin Exp Res. 1989;13(6):795–6.
126. Bier AM, Marcon L, Hakes BF, Robaie B. Effects of chemotherapeutic agents for testicular cancer on the male rat reproductive system, spermatozoa, and fertility. J Androl. 2006;27(2):189–200.
127. Bielawska DM, Zaher FM, Svinarch DM, Abel EL. Paternal alcohol exposure affects sperm cytokine mRNAexpression levels. Alcohol Clin Exp Res. 2002;26(3):547–51.
128. Bohacek J, Farinelli M, Mirante O, Steiner G, Gapp K, Coiret G, Ebeling M, Bielawski DM, Abel EL. Acute treatment of paternal alcohol exposure produces malformations in offspring. Alcohol. 1997;14(4):397–401.
129. Bohacek J, Farinelli M, Mirante O, Steiner G, Gapp K, Coiret G, Ebeling M, Bielawski DM, Abel EL. Paternal alcohol consumption affects sperm cytokine mRNAexpression levels. Alcohol Clin Exp Res. 2002;26(3):547–51.
130. Bondarenko LB, Shayakhmetova GM, Byshovets TF, Kovalenko VM, Bondarenko LB, Shayakhmetova GM, Byshovets TF, Kovalenko VM. Paternal alcohol exposure affects spermatogenesis and testicular growth. Poult Sci. 1996;75(6):767.
131. Bonduriansky R, Head M. Maternal and paternal conditional effects on offspring phenotype in Telostylinus argenticulus (Diplidae : Neriidae). J Evol Biol. 2007;20(6):2379–88.
132. Borges CDS, Pacheco TL, da Silva KP, Fernandes FH, Gregory M, Pupo AS, DMF S, Cyr DG, WDG K. Betamethasone causes intergenerational reproductive impairment in male rats. Reprod Toxicol. 2017;71:108–17.
133. Bramwell RK, McDaniel CD, Burke WH, Wilson JL, Howarth B. Influence of male broiler breeder dietary energy intake on reproduction and progeny growth. Poult Sci. 1996;75(6):267–75.
134. Breslav A, Lindeman B, Bruborg G, Duale N. Paternal benz(a)pyrene exposure modulates microRNA expression patterns in the developing mouse embryo. Int J Cell Biol. 2012.
135. Bromfield JJ, Schjenken JE, Chin PY, Care AS, Jasper MJ, Robertson SA. Paternal lesion phenotype in offspring of males subjected to postnatal stress. Mol Psychiatry. 2015;20(3):621–31.
136. Bondarenko LB, Shayakhmetova GM, Byshovets TF, Kovalenko VM, Bondarenko LB, Shayakhmetova GM, Byshovets TF, Kovalenko VM. Paternal alcohol exposure affects spermatogenesis and testicular growth. Poult Sci. 1996;75(6):767.
137. Buffett RF, Grace JT Jr, DiBerardino LA, Mir EA. Vertical transmission of α metabolite amino acid composition, reproductive capability and postnatal sensitization to paternal alcohol exposure. Acta Pol Pharm. 2012;69(5):843–50.
138. Beemelmanns A, Roth O. Biparental immune priming in the pipefish Synagrus typhle. Zoology. 2016;119(4):262–72.
139. Bellei AR. Incorporation of (3H)uridine by mouse embryos with abnormalities induced by parental hyperthermia. Biol Reprod. 1976;15(5):632–46.
140. Beltrame D, Di Salle E, Gavioli E, Gunnarsson K, Brugga M. Reproductive toxicity of exeremantine, an antinomual arnastatze, in rats and rabbits. Reprod Toxicol. 2001;15(2):195–213.
141. Berk RS, Montgomery RH, Hazlett ID, Abel EL. Paternal alcohol consumption: effects on oocyte response and serum antibody response to Pseudomonas aeruginosa infection in offspring. Alcohol Clin Exp Res. 1989;13(6):795–6.
142. Bier AM, Marcon L, Hakes BF, Robaie B. Effects of chemotherapeutic agents for testicular cancer on the male rat reproductive system, spermatozoa, and fertility. J Androl. 2006;27(2):189–200.
143. Bielawska DM, Zaher FM, Svinarch DM, Abel EL. Paternal alcohol exposure affects sperm cytokine mRNAexpression levels. Alcohol Clin Exp Res. 2002;26(3):547–51.
167. da Cruz RS, Carney EJ, Clarke J, Cao H, Cruz ML, Benitez C, Jin L, Fu Y, Cheng ZL, Wang Y, et al. Paternal malnutrition programs breast cancer cancer risk and tumor metabolism in offspring. Breast Cancer Res. 2018;20:99.

168. Daly HB, Stewart PW, Lunkenheimer L, Sargent D. Maternal consumption of Lake Ontario salmon in rats produces behavioral changes in tee offspring. Toxicol Ind Health. 1998;14(1):25–39.

169. Dawson BV, Robertson IGC, Wilson WR, Zwi LJ, Boys JT, Green AW. Evaluation of specific anxiety and depression behaviors in adult rats. PLoS One. 2011;6(4):e19789.

170. Dean A, van den Driesche S, Wang YL, McKinnell C, Macpherson S, Eddie SL, Kinnell H, Hurtado-Gonzalez P, Chambers TJ, Stevenson K, et al. Analytic exposure in pregnant rats affects fetal germ cell development with inter-generational reproductive consequences. Sci Rep. 2016;6:19789.

171. Ding S, Fan Y, Zhao N, Yang H, Ye X, He D, Jin X, Liu Q, Tian L, Li H, et al. High-fat diet aggravates glucose homeostasis disorder caused by chronic exposure to bisphenol A. J Endocrinol. 2014;221(1):167–79.

172. Ding TB, Mokhtaghamd S, Rinaudo PF, Osteen KG, Bruner-Tran KL. Paternal developmental toxicant exposure is associated with epigenetic modulation of sperm and placental Pgr and Igf2 in a mouse model. Biol Reprod. 2018;99(4):684–76.

173. Dobrzyń MK, Gajowik A, Radzikowska J, Tyrlit EJ, Jankowska-Stefea E. Male-mediated F1 effects in mice exposed to bisphenol A, either alone or in combination with X-irradiation. Mutat Res Genet Toxicol Environ Mutagen. 2015;789:36–45.

174. Dobrzyń MK, Tyrlit EJ, Pachocki KA. Developmental toxicity in mice following paternal exposure to di-N-butyl-phthalate (DBP). Biomed Environ Sci. 2011;24(5):569–78.

175. Duan MN, Xiong DQ, Bai X, Gao YL, Xiong YJ, Ding GH, Gapp K, Bohacek J, Grossmann J, Bruner AM, Manuella F, Nanni P, Mansuy IM. Potential of environmental enrichment to prevent transgenerational effects of paternal trauma. Neuropsychopharmacology. 2016;41(11):2749–58.

176. Duan MN, Xiong DQ, Yang MY, Xiong YJ, Ding GH. Parental exposure to heavy fuel oil induces developmental toxicity in offspring of the sea urchin Strongylocentrotus intermedius. Ecotoxicol Environ Saf. 2018;159:109–19.

177. Ducatez S, Baguette M, Stevens VM, Le Gré R, Fréville H. Complex interactions between paternal and maternal effects: parenteral experience and age at reproduction affect fecundity and offspring performance in a butterfly. Evol. 2011;266(11):3558–69.

178. Etterson JR, Galloway LF. The influence of light on paternal plants in Campanula americana (Campanulaceae): pollen characteristics and offspring traits. Am J Bot. 2002;89(12):1899–906.

179. Evans JP, Lymberry RA, Wild KS, Rahman MM, Gasparini C. Sperm as moderators of environmentally induced effects in a livebearing fish. Biol Lett. 2017;13(13):20170087.

180. Falci-Tebas F, Kuang J, Arceri C, Kerris JP, Andrikopoulos S, Marin EC, Gasparini C, Lu CC, Dingemanse NJ, Tuni C. Paternal-effects in a terrestrial model ectotherm are temperature dependent but no evidence for adaptive effects. J Appl Toxicol. 2001;21(2):121–39.

181. Fantasia E, Thomas M, Boyles T. Paternal trauma is exacerbated by their exposure to an “obesogenic” diet. Physiol Rep. 2015;3(3):e12336.

182. Fantelles CC, Guido LN, Rosim MP, Andrade FO, Jin L, Inchauspe J, Pires VC, de Castro IA, Hilakivi-Clarke L, de Assis S, et al. Paternal programming of breast cancer risk in daughters in a rat model: opposing effects of animal- and plant-based high-fat diets. Breast Cancer Res. 2016;18(17):1.

183. Fox CW, Bush ML, Wallin WG. Maternal age affects offspring lifespan of the seed beetle, Callosobruchus maculatus. Funct Ecol. 2003;17(6):811–20.

184. Friedman S, Larsen MD, Magnusson B, Jaalving LR, de Silva P, Nærgård BM. Paternal use of azathioprine/6-mercaptopurine or methotrexate within 3 months before conception and long-term health outcomes in the offspring—a nationwide cohort study. Reprod Toxicol. 2017;73:196–200.

185. Fulst T, McPherson ND, Owens JA, Kang WX, eman LY, Lane M. Paternal obesity induces metabolic and sperm disturbances in male offspring that are exacerbated by their exposure to an "obesogenic" diet. Physiol Rep. 2016;53(3):e12336.

186. Fulst T, Teague EMCO, Palmer NO, Delblasio MJ, Mitchell M, Corbett M, Print CG, Owens JA, Lane M. Paternal obesity initiates metabolic disturbances in two generations of mice with incomplete penetrance to the F2 generation and alters the transcriptional profile of testis and sperm microRNA content. FASEB J. 2013;27(10):4226–33.

187. Furness RJ, Herrmann C, Miletie S, Keese MC. Apparent transgenerational effects of host plant in the leaf beetle Ophraella culla (Coleoptera: Chrysomelidae). Oecologia. 1993;96(3):365–72.

188. Gapp K, Bohacek J, Grossmann J, Bruner AM, Manuella F, Mansuy IM. Potential of environmental enrichment to prevent transgenerational effects of paternal trauma. Neuropsychopharmacology. 2016;41(11):2749–58.

189. García-Palomares S, Navarro S, Pertusa JF, Herrmenegildo C, García-Pérez MA, Rausell F, Cano A, Tarín JJ. Delayed fatherhood in mice decreases reproductive fitness and longevity of offspring. Biol Reprod. 2009;80(2):345–9.

190. Gasparini C, Dosselli R, Evans JP. Sperm storage by males causes changes in sperm phenotype and influences the reproductive fitness of males and their sons. Evol Lett. 2017;1(1):16–25.

191. Gasparini C, Lu CC, Dingemansse NJ, Tuni C. Paternal-effects in a terrestrial ectotherm are temperature dependent but no evidence for adaptive effects. Funct Ecol. 2018;32(4):1011–21.

192. Ghasemi N, Babaei H, Azizali S, Kheirand. A. Effect of long-term administration of zinc on scrotal heating on mice spermatogenesis and subsequent offspring quality. Andrologia. 2009;41(4):222–8.

193. Glad T, Scharf I. Separation between maternal and paternal effects on offspring following exposure of adult red flour beetles to two stressors. Ecol Entomol. 2019;44:494–501.

194. Gill-Sharma MK, Balasiner N, Parte P, Almeen M, Junes H. Effects of tansoxin metabolites on fertility of male rat. Contraception. 2001;63(2):103–9.

195. Gomes J, Lloyd OL. Oral exposure of mice to formulations of Xenopus laevis: bovine con A, cadmium and ethylene glycol monomethyl ether. J Appl Toxicol. 2001;21(1):41–52.

196. Dunn MN, Xiong DQ, Yang MY, Xiong YJ, Ding GH. Parental exposure to heavy fuel oil induces developmental toxicity in offspring of the sea urchin Strongylocentrotus intermedius. Ecotoxicol Environ Saf. 2018;159:109–19.

197. Etterson JR, Galloway LF. The influence of light on paternal plants in Campanula americana (Campanulaceae): pollen characteristics and offspring traits. Am J Bot. 2002;89(12):1899–906.

198. Evans JP, Lymberry RA, Wild KS, Rahman MM, Gasparini C. Sperm as modernizers of environmentally induced effects in a livebearing fish. Biol Lett. 2017;13(13):20170087.

199. Falcão-Tebas F, Kuang J, Arceri C, Kerris JP, Andrikopoulos S, Marin EC, McConnell GR. Four weeks of exercise early in life reprograms adult skeletal muscle muscle insulin resistance caused by a paternal high-fat diet. J Physiol. 2019;597(1):121–36.

200. Fan Y, Ding SB, Ye XL, Manyande A, He DL, Zhao NN, Yang HQ, Jin X, Liu J, et al. Does preconception paternal exposure to a physiologically relevant level of bisphenol A alter spatial memory in an adult rat? Horm Behav. 2013;64(4):598–604.

201. Fan Y, Tan C, Liu QJ, Chen JY, Zhang H, Zhuo LK, Li TBA, Zhang Y, Ding SB, He DL, et al. Preconception paternal bisphenol A exposure induces sex-specific anxiety and depression behaviors in adult rats. PLoS One. 2018;13(2):e0192434.

202. Favero AM, Weis SN, Stangerlin EC, Rocha JBT, Nogueira CW. Sub-chronic exposure of adult male rats to diphenyl ditelluride did not affect the development of their progeny. Food Chem Toxicol. 2007;45(5):859–62.

203. Favero AM, Weis SN, Stangerlin EC, Zeni G, Rocha JBT, Nogueira CW. Adult male rats sub-chronically exposed to diphenyl diselenide: effects on their progeny. Reprod Toxicol. 2007;23(1):19–23.

204. Foytich MJ, Fodorus B, Aihbom A. Paternal occupational exposure to magnetic fields and childhood cancer (Sweden). Cancer Causes Control. 2000;11(2):151–6.

205. Finegerth A, Homanics GE. Paternal alcohol exposure reduces alcohol drinking and increases behavioral sensitivity to alcohol selectively in male offspring. PLoS One. 2014;9(6):e99078.
210. Halsey MJ, Green CJ, Monk SJ, Donc D, Knight JF, Luff NP. Maternal and paternal chronic exposure to enfuranle and halothane: fetal and histological changes in the rat. Br J Anaesth. 1981;53(3):203–15.
211. Hammill KM, Fraa S, Lee AH, Wilson JY. The effects of parental carbamazepine and gemfibrozil exposure on sexual differentiation in zebrafish (Danio rerio). Environ Toxicol Chem. 2018;37(6):1696–706.
212. Harker A, Carroll C, Raza S, Kolb B, Gribb R. Preconception paternal stress in rats alters brain and behavior in offspring. Neuroscience. 2018;388:474–85.
213. Harker A, Raza S, Williamson K, Kolb B, Gribb R. Preconception paternal stress in rats alters dendritic morphology and connectivity in the brain of developing male and female offspring. Neuroscience. 2015;303:200–10.
214. Harris EP, Allardice HA, Schenk AK, Rissman EF. Effects of maternal or paternal bisphenol A exposure on offspring behavior. Horm Behav. 2018; 101:68–76.
215. Hazlett LD, Barrett RP, Berk RS, Abel EL. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
216. Halsey MJ, Green CJ, Monk SJ, Donc D, Knight JF, Luff NP. Maternal and paternal chronic exposure to enfuranle and halothane: fetal and histological changes in the rat. Br J Anaesth. 1981;53(3):203–15.
217. Holson RR, Bates HK, LaBorde JB, Hansen DK. Behavioral teratology and exposure to quaternary ammonium disinfectants causes neural tube defects in rats. Neurotoxicol Teratol. 2006;28(2):198–209.
218. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
219. Hehar H, Ma I, Mychasiuk R. Intergenerational transmission of paternal epigenetic marks: mechanisms influencing susceptibility to post-concussion symptomology in a rodent model. Sci Rep. 2017;7:7171.
220. Hrubec TC, Melin VE, Shea CS, Ferguson EE, Garofola C, Repine CM, Odell MW, Kohler KE, Rissman EF. Maternal alcohol consumption increase offspring susceptibility to Pseudomonas aeruginosa ocular infection. Ophthal Res. 1989;215(3):381–7.
221. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
222. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
223. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
224. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
225. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
226. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
227. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
228. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
229. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
230. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
231. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
232. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
233. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
234. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
235. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
236. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
237. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
238. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
239. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
240. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
241. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
242. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
243. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
244. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
245. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
246. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
247. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
248. Hehar H, Yu K, Ma I, Mychasiuk R. Paternal age and diet: the contributions whose sires were exposed to alcohol. Dev Brain Res. 2004;149(2):103–10.
tetrachlorodibenzo-p-dioxin and birth outcomes of offspring: birth weight, preterm delivery, and birth defects. Environ Health Persp. 2004;112(14):1403–8.

256. Le Comet C, Fervers B, Pukälä E, Tynes T, Fychting M, Hansen J, Togawa K, Nordby KC, Dalton SO, Jukulsairne S, et al. Paternal occupational exposure to organic solvents and testicular germ cell tumors in their offspring: NORD-TEST study. Environ Health Persp. 2017;125(6):067023.

257. Leão VF, Raimundo JM, Ferreira LLDM, Santos-Silva JC, Vettorazzi JF, Bonfleur ML, Cameiro EM, Ribeiro RA. Effects of paternal hypothalamic obesity and tauire supplementation on adiposity and vascular reactivity in rat offspring. Adv Exp Med Biol. 2015;803:749–63.

258. Leconte V, Maloney CA, Wang KW, Morris MJ. Effects of paternal obesity on growth and adiposity of rat male offspring. Am J Physiol Endocrinol Metab. 2017;312(2):E167–25.

259. Ledig M, Misslin R, Vogel E, Holownia A, Copin JC, Tholey G. Paternal alcohol exposure: developmental and behavioral effects on the offspring of rats. Neuropharmacology. 1998;37(5):57–66.

260. Lee S, Lee MS, Park J, Zhang JY, Jin DI. Oxidative stress in the testis induced – results in lower fetal body weights. Birth Defects Res B Dev Reprod Toxicol. 2014;81:126.

261. Leite GAA, Figueiredo TM, Pacheco TL, Guerra MT, Anselmo-Franci JA, Rutkowska et al. BMC Biology.

262. Lee S, Lee MS, Park J, Zhang J, Jin DI. Oxidative stress in the testis induced – results in lower fetal body weights. Birth Defects Res B Dev Reprod Toxicol. 2014;81:126.

263. Liang F, Diao L, Jiang N, Zhang J, Wang HJ, Zhou WH, Huang GY, Ma D. Paternal ethanol exposure and behavioral abnormities in offspring: associated alterations in imprinted gene methylation. Neuropharmacology. 2014;81(1):126–33.

264. Little BB, Rigsby CH, Little LR. Pilot and astronaut offspring: possible G-force deficiency and supplementation on reproductive outcomes and imprinted gene methylation. Mol Hum Reprod. 2017;23(7):461–77.

265. Magiafoglou A, Hoffmann AA. Cross-generation effects due to cold exposure in Drosophila serrata. Funct Ecol. 2003;17(5):664–72.

266. Mankes RF, Lefevre R, Benitzen KF, Rosenblum I, Bates H, Walker AT, Abraham R, Rockwood W. Paternal effects of ethanol in the Long-Evans rat. J Toxicol Environ Health. 1982;10(6):871–8.

267. Manners MT, John NL, Lahens NF, Grant GR, Bartolomei MS, Blendy JA. Transgenerational inheritance of chronic adolescent stress: effects of stress response and the amygdala transcriptome. Genes Brain Behav. 2019;18(21493).

268. Mao Z, Xia W, Chang H, Huo W, Li Y, Xu S. Paternal BPA exposure in early life alters Igf2 epigenetic status in sperm and induces pancreatic impairment in rat offspring. Toxicol Lett. 2015;253(3):30–8.

269. Maselli J, Hales BF, Curley JP, Champagne FA. Paternal social enrichment effects on maternal behavior and offspring growth and adiposity of male rat offspring. Adv Exp Med Biol. 2015;803:749

270. Mashoodh R, Franks B, Curley JP, Champagne FA. Paternal social enrichment effects on maternal behavior and offspring growth. Proc Natl Acad Sci U S A. 2012;109:17232–8.

271. McConaha ME, Ding T, Lucas JA, Arora JA, Osteen KG, Bruner-Tran KL. Preconception omega-3 fatty acid supplementation of adult male mice with a history of developmental 3,7,8-tetrachlorodibenzo-p-dioxin exposure prevents preterm birth in unexposed female partners. Reproduction. 2014;114(2):235–41.

272. McCoy CR, Jackson NL, Brewer RL, Moughney MM, Smith DL Jr, Clinton SW. A paternal methyl donor depleted diet leads to increased anxiety- and depression-like behavior in adult rat offspring. Biosci Rep. 2018;38(55079).

273. McPherson NO, Bell VG, er-Fox DL, Fullston T, Wu LL, Robker RL, Lane M. Preconception omega-3 fatty acid supplementation of adult male mice with a history of developmental 3,7,8-tetrachlorodibenzo-p-dioxin exposure prevents preterm birth in unexposed female partners. Reproduction. 2014;114(2):235–41.

274. Rutfowska et al. BMC Biology.
offspring for low energy expenditure and increased risk for obesity in mice. FASEB J. 2016;30(2):775–84.

297. Mychasiuk R, Harker A, Iñżyński S, Gibb R. Paternal stress prior to conception alters DNA methylation and behaviour of developing rat offspring. Neuroscience. 2013;241:100–5.

298. Mychasiuk R, Zahir S, Schmold N, Iñżyński S, Kovalchuk G, Gibb R. Paternal enrichment and offspring development: modifications to brain, behavior and the epigenome. Behav Brain Res. 2012;228(2):294–8.

299. Nelson BK, Brightwell WS, Burg JR, Massari VJ. Behavioral and neurochemical alterations in the offspring of rats after paternal or maternal prenatal exposure to the industrial solvent 2-methyloctanol. Pharmacol Biochem Behav. 1984;20(2):269–79.

300. Nelson BK, Brightwell WS, Mackenzie-Taylor DR, Burg JR, Massari VJ. Neurochemical, but not behavioral, deviations in the offspring of rats following prenatal or paternal prenatal exposure to ethanol. Neurotoxicol Teratol. 1988;10(1):15–22.

301. Nelson BK, Brightwell WS, Robertson SK, Khan A, Krieg EF, Jr, Massari VJ. Behavioral teratology investigation of 1-butanol in rats. Neurotoxicol Teratol. 1990;11(3):313–5.

302. Niknazar S, Nahavij A, Peyvai AA, Peyvai H, Razzolini L, Rutkowska et al. BMC Biology.

303. Nunes JC, Metcalf NB, Monaghan P. Experimental demonstration that offspring fathered by old males have shorter telomeres and reduced lifespan. Proc R Soc B Biol Sci. 2018;285(20182068).

304. Nygaard UC, Hansen JS, Groeng EC, Melkild I, Løvik M. Suppression of paternal stress effects in rat offspring. Behav Brain Res. 2017;324:71–8.

305. Oakes DJ, Webster WS, Brown-Woodman PDC, Ritchie HE. A study of the potential for a herbeicide formulation containing 2,4-D and picloram to cause male-mediated developmental toxicity in rats. Toxicol Sci. 2002;68(1):200–6.

306. Omeñales F, Bringheti I, Mattos BANF, arim-de-Lacerda CA, Aguila MB. Father’s obesity programs the adipoic tissue in the offspring via the local renin-angiotensin system and MAPKs pathways, especially in adult male mice. Eur J Nutr. 2018;57(5):1901–12.

307. O’Neill SM, Halford DM. Senescent characteristics, mating performance and serum testosterone in rams fed sewage solids. Theriogenology. 1985;24(1):121–33.

308. Park HS, Kim TW. Paternal physical exercise improves spatial learning ability and fertilization capacity after targeting spermatocytes and maturing offspring. Mar Environ Res. 2018;136:120–3.

309. Parent RH, Jansen E, Taylor PD, Poston L, Williamson C. Paternal cholestasis exacerbates the evolution of aging. Evolution. 2002;56(5):927–35.

310. Parent RH, Jansen E, Taylor PD, Poston L, Williamson C. Paternal stress effects in rat offspring. Behav Brain Res. 2017;324:71–8.

311. Parent RH, Klein V, Beemelmanns A, Scharsack JP, Reusch TBH. Male pregnancy and biparental immune priming. Am Nat. 2012;180(6):802–14.

312. Ryan DP, Henzel KS, Pearson BL, Swiek ME, Papazoglou A, Guo L, Paesler K, Yu M, Müller R, Xie K, et al. A paternal methyl donor-rich diet altered cognitive and neural functions in offspring mice. Mol Psychiatry. 2018;23(5):1345–55.

313. Rawat A, Guo J, Renoir T, Pang TY, Hansen AJ. Hyperresponsitvity to serotonin in the absence of hippocampal 5-HT1AR and 5-HTT gene expression changes following paternal corticosterone treatment. Environ Epigenetics. 2018;4(2):day015.

314. Santavirta T, Santavirta N, Gilman SE. Association of the World War II Finnish evacuation of children with psychiatric hospitalization in the next generation. JAMA Psychiatry. 2018;75(1):21–7.

315. Schade FM, Clemmesen C, Wegner KM. Within-and transgenerational effects of ocean acidification on life history of marine three-spined stickleback (Gasterosteus aculeatus). Mar Biol. 2014;161(7):1667–76.

316. Schmid B, Dolt C. Effects of maternal and paternal environment and genotype on offspring phenotype in Solidago altissima L. Evolution. 1994;48(5):1525–49.

317. Schmidth T, Lawrence CC, Whelan EA, Dankovic DA, Deddens JA, Pacieltta LA, Reefhuis J, Sweeney MH, Connally LB, Fornwald L, et al. Ontogeny-driven rDNA rearrangement, methylation, and transcription, and paternal influence. PLoS One. 2011;6(7):e22266.

318. Scholz S, Dott S, Henrich D, Haidinger K, Pfeifer A, Wiederlack A, et al. Male mediated developmental toxicity in rats. Toxicol Sci. 2002;68(1):200–6.

319. Schumacher JM, Hansen JS, Groeng EC, Melkild I, Løvik M. Suppression of paternal-specific Irgc in offspring after preconceptional immunisation. Scand J Immunol. 2013;77(2):92–103.

320. Ricci E, Noli S, Cipriani S, La Vecchia I, Chiaffarino F, Ferrari S, Mauri PA, Rischner M, Fedele L, Parazzini F. Maternal and paternal caffeine intake and ART outcomes in couples referring to an Italian fertility clinic: a prospective cohort. Nutrients. 2018;10(8):1116.

321. Robledo CA, Yeung E, Mendola P, Sundaram R, Maisog J, Sweeney AM, Barr DB, Buck Louis GM. Preconception maternal and paternal exposure to persistent organic pollutants and birth size: the LIFE study. Environ Health Perspect. 2015;123(1):88–94.

322. Rompala GR, Finigere A, Homanics GE. Paternal preconception ethanol exposure exposure blunts hypothalamic-pituitary-adrenal axis responsivity and stress-induced excessive fluid intake in male mice. Alcohol. 2016;53:19–25.

323. Rompala GR, Finigere A, Slater M, Homanics GE. Paternal preconception alcohol exposure imparts intergenerational alcohol-related behaviors to male offspring on a pure C57BL/6J background. Alcohol. 2017;60:169–77.

324. Roth O, Joop G, Eggert H, Hilbert J, Daniel J, Schmid-Hempel P, Kurtz J. Paternally derived immune priming for offspring in the red flour beetle, Tribolium castaneum. J Anim Ecol. 2010;79(2):403–13.

325. Roth O, Klein V, Beemelmanns A, Scharsack JP, Reusch TBH. Male pregnancy and biparental immune priming. Am Nat. 2012;180(6):802–14.

326. Ryan DP, Henzel KS, Pearson BL, Swiek ME, Papazoglou A, Guo L, Paesler K, Yu M, Müller R, Xie K, et al. A paternal methyl donor-rich diet altered cognitive and neural functions in offspring mice. Mol Psychiatry. 2018;23(5):1345–55.

327. Rawat A, Guo J, Renoir T, Pang TY, Hansen AJ. Hyperresponsitvity to serotonin in the absence of hippocampal 5-HT1AR and 5-HTT gene expression changes following paternal corticosterone treatment. Environ Epigenetics. 2018;4(2):day015.

328. Santavirta T, Santavirta N, Gilman SE. Association of the World War II Finnish evacuation of children with psychiatric hospitalization in the next generation. JAMA Psychiatry. 2018;75(1):21–7.

329. Schade FM, Clemmesen C, Wegner KM. Within- and transgenerational effects of ocean acidification on life history of marine three-spined stickleback (Gasterosteus aculeatus). Mar Biol. 2014;161(7):1667–76.

330. Schmid B, Dolt C. Effects of maternal and paternal environment and genotype on offspring phenotype in Solidago altissima L. Evolution. 1994;48(5):1525–49.

331. Schomisch T, Lawrence CC, Whelan EA, Dankovic DA, Deddens JA, Pacieltta LA, Reefhuis J, Sweeney MH, Connally LB, Fornwald L, et al. Ontogeny-driven rDNA rearrangement, methylation, and transcription, and paternal influence. PLoS One. 2011;6(7):e22266.
small noncoding RNA profile in sperm and modifies anxiety and depressive phenotypes in the offspring. Transl Psychiatry. 2016;6:e6817.

30. Short AK, Yeshurun S, Powell R, Perreau VM, Fox A, Kim JH, Pang TY, Hanan AJ. Exercise alters mouse sperm small noncoding RNAs and induces a transgenerational modification of male offspring conditioned fear and anxiety. Transl Psychiatry. 2017;7(5):e1114.

31. Shu XO, Stewart P, Wen WQ, Han DH, Potter JD, Buckley D, Heineman E, Robison LL. Parental occupational exposure to hydrocarbons and risk of acute lymphocytic leukemia in offspring. Cancer Epidemiol Biomark Prev. 1999;8(10):783–91.

32. Silva PVE, da Silva RF, Borges CD, Cavaniari MM, Francia C, Barbosa F, Kemptinas WD. Sexual differentiation and reproductive development of female rat offspring after paternal exposure to the anti-tumor pharmaceutical cisplatin. Reprod Toxicol. 2016;60:112–22.

33. Smith RG, Fernandes C, Kember R, Schalkwyk LC, Busbaum J, Reichenberg A, Miller J. Transcriptomic changes in the frontal cortex associated with paternal age. Mol Autism. 2014;5:24.

34. Smith RG, Kember RL, Miller J, Fernandes C, Schalkwyk LC, Busbaum JD, Reichenberg A. Advancing paternal age is associated with deficits in social and exploratory behavior in the offspring of a mouse model. PLoS One. 2009;4(12):e8456.

35. Soubry A, Murphy SK, Wang F, Huang Z, Vidal AC, Fuemmerle BF, Kurtzberg J, Murtha A, Jittle RL, Schildkraut JM, et al. Newborns of obese parents have altered DNA methylation patterns at imprinted genes. Int J Obes. 2015;39(4):650–70.

36. Soyka LF, Joffe JM, Peterson JM, Smith SM. Chronic methadone administration to male rats: tolerance to adverse effects on sires and their progeny. Pharmacol Biochem Behav. 1978;45(3):797–807.

37. Spindler C, Segabirani E, De Meireles ALF, Piazza FY, Mega F, Salvaaggio GD, Achava M, Bleser VR, Marcuzzo S. Paternal physical exercise modulates global DNA methylation status in the hippocampus of male rat offspring. Neural Regen Res. 2018;13(4):491–500.

38. Steele EJ. Observations on offspring of mice made diabetic with streptozocin. Diabetes. 1978;27(3):79–87.

39. Terasima M, Barbour S, Ren J, Yu W, Han Y, Muegge K. Effect of high fat diet on paternal sperm histone distribution and male offspring liver gene expression. Epigenetics. 2015;10(9):161–71.

40. Tornqvist S. Paternal work in the power industry: effects on children at delivery. J Occup Environ Med. 1998;40(2):111–7.

41. Triggs AM, Knill RJ. Parental diet has strong transgenerational effects on offspring immune function. Funct Ecol. 2012;26(6):1409–17.

42. Ueker ME, Silva VM, Moi GP, Pignati WA, Mattos IE, Silva AMC. Parenteral administration to male rats affects learning function of murine progeny. Anesth Analg. 2018;127(3):491–500.

43. Steele EJ. Observations on offspring of mice made diabetic with streptozocin. Diabetes. 1978;27(3):79–87.

44. Tang CK, Chalon J, Markham JP, Ramanathan S, Turndorf H. Exposure of sires to estrus enflurane affects learning function of murine progeny. Anesth Analg. 1984;63(3):729–80.

45. Terashima M, Barbour S, Ren J, Yu W, Han Y, Muegge K. Effect of high fat diet on paternal sperm histone distribution and male offspring liver gene expression. Epigenetics. 2015;10(9):161–71.

46. Torrens R. Paternal work in the power industry: effects on children at delivery. J Occup Environ Med. 1998;40(2):111–7.

47. Triggs AM, Knill RJ. Parental diet has strong transgenerational effects on offspring immune function. Funct Ecol. 2012;26(6):1409–17.

48. Ueker ME, Silva VM, Moi GP, Pignati WA, Mattos IE, Silva AMC. Parenteral administration to male rats affects learning function of murine progeny. Anesth Analg. 2018;127(3):491–500.

49. Vallaster MP, Kukreja S, Bing XY, Ngolab J, Zhao-Shea RB, Gardner PD, Triggs AM, Knell RJ. Parental diet has strong transgenerational effects on offspring development time, adult body size and metabolism in offspring. Elife. 2017;6:e24771.

50. Weyrich A, Benz S, Karl S, Jeschek M, Jegewie K, Pickel J. Paternal heat exposure causes DNA methylation and gene expression changes of Stat3 in wild guinea pig sires. EcoV. 2016;69:2657–66.

51. Weyrich A, Jeschek M, Schraper KT, Lenz D, Chung TH, Rubensam K, Vasar S, Schneemann M, Ortman S, Jegewie K, et al. Diet changes alter paternally inherited epigenetic pattern in male wild guinea pigs. Environ Epigenetics. 2018;4(2):dyv011.

52. Weyrich A, Lenz D, Pickel J. Environmental change-dependent inherited epigenetic response. Genes. 2019;10(1):4.

53. Weyrich A, Lenz D, Jeschek M, Chung TH, Rubensam K, Göritz F, Jegewie K, Pickel J. Paternal intergenerational epigenetic response to heat exposure in male wild guinea pigs. Mol Ecol. 2016;25(8):1729–40.

54. White SL, Vassoler FM, Schmidt HD, Pierce RC, Wimmer ME. Enhanced anxiety in the male offspring of sires that self-administered cocaine. Addict Biol. 2016;21(4):802–10.

55. Wimmer ME, Pat LA, Fant B, Guercio LA, Areola AC, Schmidt HD, Sildo S, Han Y, Garcia BA, et al. Paternal cocaine taking elicits epigenetic remodeling and memory deficits in male progeny. Mol Psychiatry. 2017;22(11):1641–50.

56. Wimmer ME, Vassoler FM, White SL, Schmidt HD, Sildo S, Han Y, Garcia BA, Pierce RC. Impaired cocaine-induced behavioral plasticity in the male offspring of cocaine-experienced sires. Eur J Neurosci. 2019;49(9):1115–1126.

57. Windham GC, Fernler L, Swan SH. Maternal and paternal alcohol consumption and the risk of spontaneous abortion. Epidemiology. 1992;3(4):364–70.

58. Wu L, Lu Y, Xiao Y, Liu B, Li S, Li Y, Xing F, Chen D, Liu X, Zhao J, et al. Paternal psychological stress reprograms hepatic gluconeogenesis in offspring. Cell Metab. 2016;23(4):735–43.

59. Xia RL, Jin LM, Li DK, Liang H, Yang F, Chen JP, Yuan W, Mao MH. Association between paternal alcohol consumption before conception and anogenital distance of offspring. Alcohol Clin Exp Res. 2018;42(4):735–42.

60. Xie K, Ryan DP, Pearson BL, Henkel KS, Neff F, Vidal RO, Hennion M, Lehmann I, Schleif M, Schröder S, et al. Epigenetic alterations in longevity regulators, reduced life span, and exacerbated aging-related pathology in old father offspring mice. Proc Natl Acad Sci U S A. 2018;115(10):E2348–57.

61. Yang F, Chen J, Mao MH, Yuan W, Li L, Liang H, Ehrenstein V, Li J. Risk of autism spectrum disorder in offspring following paternal use of selective serotonin reuptake inhibitors before conception: a population-based cohort study. BMJ Open. 2017;7(12):e016368.
435. Goldberg LR, Gould TJ. Multigenerational and transgenerational effects of paternal exposure to drugs of abuse on behavioral and neural function. Eur J Neurosci. 2019;50(3):2453–2466.

436. Gottesfeld Z, Abel EL. Maternal and paternal alcohol use: effects on the immune system of the offspring. Life Sci. 1991;48(1-7):1–8.

437. Hales BF, Robaire B. Paternal exposure to drugs and environmental chemicals: effects on progeny outcome. J Androl. 2001;22(6):927–36.

438. Hales BF, Robaire B. The male germ cell as a target for toxicants. In: McQueen CA, ed. Comprehensive Toxicology Kildlington, United Kingdom Elsevier Ltd 2010:115–29.

439. Hannan AJ. Stressing the seminal role of paternal experience in transgenerational 'epigenopathy' affecting offspring health and disease susceptibility. Neuroscience. 2018;388:472–3.

440. Mine C. A paternal diet for offspring success? Sci Transl Med. 2017;9(386):eaan2780.

441. Holland ML, Rakyan VK. Transgenerational inheritance of non-genetically determined phenotypes. Biochem Soc Trans. 2013;41(3):769–76.

442. Hwang K, Gittens P, Avila D, Jr., Lipshultz LI. Impact of paternal exposure to antirheumatic drugs (retinoids, immune suppressants, ant androgens and thalidomide) on sperm and offspring phenotypes. Curr Opin Endocrinol Diab Obes. 2017;24(1):47–55.

443. James WH. Offspring sex ratios at birth as markers of paternal endocrine disruption. Environ Res. 2006;100(1):77–85.

444. Jenkins TG, Aston KI, Meyer T, Carrell DT. The sperm epigenome, male aging, and potential effects on the embryo. Adv Exp Med Biol. 2015;868:81–93.

445. Jenkins TG, Carrell DT. The sperm epigenome and potential implications for the developing embryo. Reproduction. 2012;143(6):727–34.

446. Kaati G. Case studies on epigenetic inheritance. In: Epigenetics and Human Health, AG. Harlberger (Ed). 2010: 63–86.

447. Karakezi MA, Deysyris N, Thomopoulos TP, Ntouvelis E, Kantzouan M, Diamantaras AA, Moschovi M, Baka M, Hatzipetalis E, Kouriit M, et al. Parental alcohol consumption and risk of leukemia in the offspring: a systematic review and meta-analysis. Eur J Cancer Prev. 2017;26(5):433–41.

448. Kaschem MA, Lee A, Pow DV, Sery O, Balcar VJ. Could ethanol-induced alterations in mRNAs for glutamate transporter in testes contribute to the effect of paternal drinking on the risk of abnormalities in the offspring? Med Hypotheses. 2017;95:857–9.

449. Kimmis S. Expanding waistlines heighten the risk for reproductive toxicity. Biol Reprod. 2010;82(1):1–3.

450. Klattakuk LP, Bak ST, Nielsen AL. The influence of paternal diet on sncRNA-epigenetic inheritance. Mol Gen Genomics. 2019;294(1):1–11.

451. Kumar M, Kumar K, Jain S, Hassan T, Dada R. Novel insights into the genetic and epigenetic paternal contribution to the human embryo. Clinics. 2013;68:14–15.

452. Kumar P, Das A, Lal NR, Jain S, Ghosh A. Safety of important dermatological drugs (retinoids, immune suppressants, anti androgens and thalidomide) in reproducitively active males with respect to pregnancy outcome: a brief review of literature. Ind J Dermatol Venereol Leprol. 2018;84(3):539–46.

453. Li J, Tsypyrkov O, Yang X, Hocher B. Paternal programming of offspring cardiometabolic diseases in later life. J Hypertens. 2016;34(11):2111–26.

454. Liu YS. Telegony, the sire effect and non-Mendelian inheritance mediated by spermatozoa; a historical overview and modern mechanistic speculations. Reprod Domest Anim. 2011;46(2):338–43.

455. Loche E, Ozanne SE. Non-genetic transmission of obesity - it’s in your epigenes. Trends Endocrinol Metab. 2016;27(6):349–50.

456. Lucas ES, Watkins AJ, Fazeli A, Holt WV. The long-term effects of the periconceptional period on embryo epigenetic profile and phenotype; the paternal role and his contribution, and how males can affect offspring’s phenotype/epigenetic profile. Adv Exp Med Biol. 2017;1014:137–54.

457. Ly L, Chan D, Trauter JM. Developmental windows of susceptibility for epigenetic inheritance through the male germline. Semin Cell Dev Biol. 2015;43:96–105.

458. Macartney EL, Crean AJ, Bonduriansky R. Epigenetic paternal effects as costly, condition-dependent traits. Heredity. 2018;121(3):248–56.

459. Manso IN, Hulan and laboratory animal test systems available for detection of reproductive failure. Prev Med. 1978:7(3):322–31.

460. Mansuy IM, Mashhoudr R, Champagne FA, Sweatt JD, Meaney MJ, Nestler EJ, Akbarian S. Transgenerational inheritance in mammals. 2013.

461. Marshall DJ. Environmentally induced (co)variation in sperm and offspring phenotypes as a source of epigenetic effects. J Exp Biol. 2015;218(1):107–13.

462. McCowan PO, Matthews SC. Prenatal stress, glucocorticoids, and developmental programming of the stress response. Endocrinology. 2018;159(1):69–82.

463. Micu MC, Otsenens M, Villiger PM, Micu R, Ionescu R. Paternal exposure to antirheumatic drugs-what physicians should know: review of the literature. Semin Arthritis Rheum. 2018;48(2):343–55.

464. Morgan CP, Chan JC, Bale TL. Driving the next generation: paternal lifetime experiences transmitted via extracellular vesicles and their small RNA cargo. Biol Psychiatry. 2019;85(2):164–71.

465. Murphy KE, Jenkins TG, Carrell DT. How the father might epigenetically program the risk for developmental origins of health and disease effects in his offspring. In: Editor(s): Cheryl S. Rosenfeld, The Epigenome and Developmental Origins of Health and Disease, Academic Press. 2015: 361–375.

466. Murdoch ME, Murdoch PJ, Carrell DT. Epigenetic changes in the paternal germline. In: Editor(s): Trygge Tollefsbol, Transgenerational Epigenetics, Academic Press. 2014: 43–55.

467. Nagao T, Takada N, Onoda N. Transgenerational teratogenesis by prenatal exposure to endocrine disrupting chemicals. Genes Environ. 2011;33(2):50–60.

468. Nanassy L, Carrell DT. Patter effects on early embryogenesis. J Exp Clin Assist Reprod. 2008;52.

469. Nelson BK, Moorman WJ, Schröder SM. Review of experimental male-unrelated behavioral and neurochemical disorders. Neurotoxicol Teratol. 1996;18(6):611–6.

470. Nieto S, Patrini MA, Nielsen DA, Kostet TA. Don’t worry; be informed about the epigenetics of anxiety. Pharmacol Biochem Behav. 2016;146:60–72.

471. Oliveira PF, Sousa M, Silva BM, Monteiro MR, Alves MG. Obesity, energy balance and spermatogenesis. Reproduction. 2017;153(6):R173–85.

472. Pacchierotti F, Spamo M. Environmental impact on DNA methylation in the germline: the state of the art and gaps of knowledge. Biomed Res Int. 2015; Article ID 123484:23 pages.

473. Pang TY, Short AK, Bredy TW, Hannan AJ. Transgenerational paternal transmission of acquired traits: stress-induced modification of the sperm regulatory transcriptome and offspring phenotypes. Curr Opin Behav Sci. 2017:14(1):140–7.

474. Pearson BL, Ehninger D. Impact of paternal nutrition on epigenetic patterns. Epigenomics. 2018;10(2):115–7.

475. Perrin M, Kleinhaus K, Opler M, Messinger J, Malapinsa D. Epidemiology research and epigenetics: translational epidemiology of schizophrenia. In: A. Petronis and J. Mill (eds), Brain, Behavior and Epigenetics, Epigenetics and Human Health, Springer-Verlag Berlin Heidelberg. 2011:71–96.

476. Pontha B, Grandjean V, Movassat J. Mother or father, who is in the front line? Mechanisms underlying the non-genomic transmission of obesity/ diabetes via the maternal or the paternal line. Nutrients. 2019;11(2):233.

477. Purd D, Dhawan J, Mishra RK. The paternal hidden agenda: epigenetic inheritance through sperm chromatin. Epigenomics. 2010;5(5):386–91.

478. Robaire B, Codrington AM, Hales BF, Anderson D, Brinkworth MH. Molecular changes in sperm and early embryos after paternal exposure to a chemotherapeutic agent. In: T.J. Anderson), RSC Publishing. 2007: 124

479. Rodgers A8, Bale TL. Germ cell origins of posttraumatic stress disorder risk: the transgenerational impact of parental stress experience. Biol Psychiatry. 2015;78(5):307–14.

480. Romanos N, Kenev P, Soubry A. Extending the developmental origins of health and disease theory: does paternal diet contribute to breast cancer risk in daughters? Breast Cancer Res. 2016;18(1):103.

481. Ronje E, Muller A, Beckhuijzen MWW, Hass U, Heinrich-Hirsch B, Paparella M, Schenk E, Ustilich B, Haikuken BC, Pieriha AH. On the impact of second
generation mating and offspring in multi-generation reproductive toxicity studies on classification and labelling of substances in Europe. Regul Toxicol Pharmacol. 2011;61(2):251–60.

487. Rowold ED, Schulze L, Van der Auwera S, Grabe HJ. Paternal transmission of early life traumatization through epigenetics: do fathers play a role? Med Hypotheses. 2017;109:59–64.

488. Pierce RC, Vassoler FM. Reduced cocaine reinforcement in the male offspring of cocaine-experienced sires. Neuropsychopharmacology. 2014;39(1):238.

489. McLain VC. Final report of the addendum to the safety assessment of n-buty1 alcohol as used in cosmetics. Int J Toxicol. 2008;27:53–69.

490. Sands K, Jansen R, Zaslav S, Greenwald D. Review article: the safety of therapeutic drugs in male inflammatory bowel disease patients wishing to conceive. Aliment Pharmacol Ther. 2015;41(9):821–34.

491. Sarkar DK. Male germ line transmits fetal alcohol epigenetic marks for multiple generations: a review. Addict Biol. 2016;21(1):23–34.

492. Savitz DA, Chen J. Parental occupation and childhood cancer: review of epidemiologic studies. Environ Health Perspect. 1990;88:325–37.

493. Schagdarsurengin U, Steger K. Epigenetics in male reproduction: effect of paternal diet on sperm quality and offspring health. Nat Rev Urol. 2016;13(10):584–95.

494. Schagdarsurengin U, Western P, Steger K, Meinhardt A. Developmental origins of male subfertility: role of infection, inflammation, and environmental factors. Semin Immunopathol. 2016;38(6):765–81.

495. Schubert C. Blame it on papa: paternal effects of diet. Biol Reprod. 2013;89(5):1086–9.

496. Sofield MD, Kalkkas PW. Forgiving the sins of the fathers. Nat Neurosci. 2013;16(1):4–5.

497. Shah PS. Paternal factors and low birthweight, preterm, and small for gestational age births: a systematic review. Am J Obstet Gynecol. 2010;202(2):103–23.

498. Sharma R, Agarwal A, Rohra VK, Asadi M, Abu-Elmagd M, Turki RF. Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring. Reprod Biol Endocrinol. 2015;13:35.

499. Sharp GC, Lawlor DA, Richardson SS. It’s the mother!: how assumptions about the causal primacy of maternal effects influence research on the developmental origins of health and disease. Soc Sci Med. 2018;213:20–7.

500. Siddiqi B, Mauduit C, Simeoni U, Benahmed M. Sperm epigenome as a marker of environmental exposure and lifestyle, at the origin of diseases inheritance. Mutat Res Rev Mutat Res. 2018;778:38–44.

501. Slijvka Y, Zhang Y, Nowak FV. Epigenetic effects of paternal diet on offspring: emphasis on obesity. Endocrine. 2014;48(1):36–46.

502. Soubry A. P0HaD: why we should study future fathers. Environ Epigenetics. 2018;4(2):dvy007.

503. Soubry A, Hoyo C, Jirtle RL, Murphy SK. A paternal environmental legacy: evidence for epigenetic inheritance through the male germ line. BioEssays. 2014;36(6):359–71.

504. Spagnolo A. Teratogenesis of alcohol. Ann Ist Super Sanita. 1993;29(1):89–99.

505. Stuppia L, Franzago M, Ballerini P, Gatta V, Antonucci I. Epigenetics and male reproduction: the consequences of paternal lifestyle on fertility, embryo development, and children lifetime health. Clin Epigenetics. 2015;7:120.

506. Taskinen HK. Effects of parental occupational exposures on spontaneous abortion and congenital malformation. Scand J Work Environ Health. 1990;16(5):297–314.

507. Terrell ML, Hartnett KP, Marcus M. Can environmental or occupational hazards alter the sex ratio at birth? A systematic review. Emerg Health Threats J. 2011;4(1):7109.

508. Tunc-Ozcan E, Sittig LJ, Harper KM, Graf EN, Redel EE. Hypothesis: genetic and epigenetic risk factors interact to modulate vulnerability and resilience to FASD. Front Genet. 2014;5:261.

509. Vanhees K, Vandenbroucke JK, van Schooten FJ, Godschalk RWL. What is what you eat, and so are your children: the impact of micronutrients on the epigenetic programming of offspring. Cell Mol Life Sci. 2014;71(2):271–85.

510. Vaughn AR, Sivamani RK, Lip PA, Shi YV. Paternal vs. maternal factors in childhood atopic dermatitis. Dermatitis. 2017;28(4):241–5.

511. Whalley K. Epigenetics: from father to son. Nat Rev Neurosci. 2011;12(10):548.

512. Wigle DT, Turner MC, Krewski D. A systematic review and meta-analysis of childhood leukemia and parental occupational pesticide exposure. Environ Health Perspect. 2009;117(10):1505–13.

513. Woestmann L, Saastamoinen M. The importance of trans-generational effects in lepidoptera. Curr Zool. 2016;62(5):489–99.

514. Yan MH, Zhai QW. Sperm tRNAs and acquired metabolic disorders. J Endocrinol. 2016;230(3):F13–8.

515. Yeshunur S, Hanhan AI. Transgenerational epigenetic influences of paternal environmental exposures on brain function and predisposition to psychiatric disorders. Mol Psychiatry. 2019;24(4):536–548.

516. Youngson NA, Whitelaw E. The effects of acquired paternal obesity on the next generation. Asian J Androl. 2011;13(2):195–6.

517. Zumudio NM, Chong SY, O’Bryan MK. Epigenetic regulation in male germ cells. Reproduction. 2008;136(2):131–46.

518. Zeisel SH. Epigenetic mechanisms for nutrition determinants of later health outcomes. Am J Clin Nutr. 2009;89(5):988S–93S.

519. Core Team R. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2020.

520. Wickham H. Ggplot2: elegant graphics for data analysis; 2009.

521. Ana M, Cuccurullo C. bibliometrix: an R-tool for comprehensive science mapping analysis. J Infometrics. 2017;11(4):659–75.

522. Nettle D, Frankenhuis WE. The evolution of life-history theory: a bibliometric analysis of an interdisciplinary research area. Proc R Soc B Biol Sci. 2019;286(1899):20190040.

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