Evolutionary Psychological Science
DOI 10.1007/s40806-016-0074-4

RESEARCH ARTICLE

Can Contraceptive Pill Affect Future Offspring's Health? The Implications of Using Hormonal Birth Control for Human Evolution

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Abstract Resistance to disease is greater for offspring if the parents have dissimilar immune systems, as their pathogen-detection ability is enhanced. Accordingly, women evolved to be sexually attracted to men with a dissimilar immune system, primarily during high-fertility cycle phases. Contraceptive pills, however, reverse women's preferences, leading them to be attracted to men with a similar immune system. In the present study ($N = 192$), we compared the health of children born to parents who met while the mother was on the pill with that of children whose parents met when the mother was not on the pill. Results confirmed our predictions, indicating that children to mothers who were on the pill are more infection-prone, require more medical care, suffer from a higher frequency of common sicknesses, and are perceived as generally less healthy than children whose parents met on non-pill circumstances. Results are discussed in light of the current antibiotic world crisis.

Keywords Children's health · Contraceptive pills · Mate choice · Menstrual cycle · MHC

People often use the expression "it smells funny to me." Research has recently indicated that when it comes to romantic partners, people should indeed follow their nose: the more they like their partner's body odor, the better the genetic fit is with respect to immune system benefits for potential children (Roberts et al. 2013). Unfortunately, the commonly used contraceptive pills may cancel out these potential benefits. When women use contraceptive pills, which imitate a state of pregnancy (Alvergne and Lummaa 2010), their natural odor preference for good-fitting romantic partners is reversed, such that they switch to preferring the odor of poorly fitting partners (Wedekind and Füri 1997; Wedekind et al. 1995). To date, it is still unclear whether this shift in mate preference affects the health of children born to couples who have met while the woman was on pills. In the present study, we examined this possibility by comparing the health of children born to parents who met while the mother was on contraceptive pills with the health of those whose mother was not on pills.

Fertility Status and Women's Mate Preferences

When choosing a partner to have children with, it is only natural to desire "Prince Charming" or "Cinderella," who may pass on their beneficial genetic qualities to future offspring. Given that better genes increase the offspring's survival and reproduction chances, theories suggest that mechanisms that detect "genetic quality" should have evolved to lead people to be sexually attracted to "knights in shining genes" (Bertram et al. 2016; Neff and Pitcher 2005). Several studies have indeed shown that during the fertile phase of the menstrual cycle, women prefer men with masculine faces, bodies, and voice (Feinberg et al. 2006; Frost 1994; Johnston et al. 2001; Penton-Voak and Perrett 2000; Penton-Voak et al. 1999; Puts 2005), which were theorized to indicate high quality genotype. Other studies, however, have indicated that "good genes" or "complementary genes" explain only a small portion of the variance in mate choice (Bertram et al. 2016; Neff and Pitcher 2005).

Another major cue for mate suitability, commonly used by mammals, is odor, which signals compatibility between potential mates' immune systems. More

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Published online: 07 November 2016

specifically, odor indicates the extent of overlapping between one's major histocompatibility complex (MHC) genes and the potential mate's MHC genes, such that more attractive odor signals less overlap between mates' MHC (Wedekind et al. 1995). MHC genes encodes cell surface receptors that play a critical role in differentiating self from non-self and initiating most immune responses, thereby regulating recognition of infectious diseases (Thornhill et al. 2003). To put it simply, the MHC is the immune system's pathogen mugshot library and face recognition software. The larger the library, the more threats the immune system can combat. Offspring would thus benefit the most from having parents with dissimilar MHC genotypes, which results in an enhanced immune system (Roberts et al. 2013).

Evidence for dissimilar MHC preference has been found in numerous species, including mice (Penn and Potts 1998; Potts et al. 1991; Yamazaki et al. 1976, 1988), fish (Aeschlimann et al. 2003; Landry et al. 2001), and birds (Bonneaud et al. 2006; Richardson et al. 2005). Among humans, however, findings are equivocal. Preference for MHC-dissimilar partners has been found in several human populations, such as the Hutterite community (Ober et al. 1997) and European Americans (Chaix et al. 2008), but not in others, such as the South Amerindian tribes (Hedrick and Black 1997) and African Americans (Chaix et al. 2008). Using the "sweaty T-shirts paradigm," in which female participants sniff T-shirts recently worn by males, studies have also shown that some women (mainly European and Asian participants) prefer the scent of MHC-dissimilar partners over that of MHC-similar partners (Jacob et al. 2002; Saphire-Bernstein et al. 2016; Wedekind and Füri 1997; Wedekind et al. 1995), but others do not (e.g., Southern Brazilian participants; Santos et al. 2005).

Research has revealed that contraceptive pill use reverses the natural preference for MHC dissimilarity, such that women who respond to MHC-related odors prefer MHC-similar partners over MHC-dissimilar partners while on contraceptive pills (Wedekind and Füri 1997; Wedekind et al. 1995). This shift in MHC preferences corresponds to the one occurring across the menstrual cycle. Theoretical accounts suggest that naturally cycling women experience male preference shift throughout their menstrual cycle (Gangestad and Thornhill 2008) that helps them obtain resources relevant to their current fertility status (fertile versus infertile). It is assumed that during the fertile phase of the menstrual cycle, women seek genetic benefits for their offspring (Gangestad and Cousins 2001) and are thus more attracted to men whose features indicate such benefits (e.g., masculine, symmetrical, and MHC-dissimilar men; B. C. Jones et al. 2008; Little et al. 2007; Roberts et al. 2008; Wedekind et al. 1995).

In contrast, during the infertile phase of the cycle, women are theorized to seek cues of high investment in parenting and partnership (Thornhill and Gangestad 2008), which are typically associated with fewer masculine features. Women tend to prefer MHC similarity during the infertile phase for similar reasons (i.e., its association with the smell of genetic relatives who may assist them during pregnancy; Thornhill et al. 2003). Because contraceptive pills introduce hormones that prevent ovulation and lead to temporary loss of fertility (Alvergne and Lummaa 2010; B. C. Jones et al. 2005; Puts 2006; Roberts et al. 2008; Wedekind et al. 1995), women's natural MHC-preference fixates on similarity as in natural infertile phases of the cycle.

Wedekind et al. (1995) were the first to document this phenomenon by asking women who were and were not on contraceptive pills to rate the odors of T-shirts worn for two consecutive nights by similarly aged men. Ratings were performed in the absence of other visual information. Their findings showed that in contrast to women who were not on pills, women using the pill rated the smell of shirts worn by MHC-similar men as more pleasant. In line with these findings, another study has revealed that normally cycling women (women who are not using contraceptive agents) tend to rate MHC-dissimilar men as more physically attractive, whereas women using contraceptive pills tend to rate MHC-similar men as more physically attractive than MHC-dissimilar men (Wedekind and Füri 1997). This research has also suggested that contraceptive pills affect not only mate preferences but also actual mate choice. In particular, women, who reported preference for an odor of a T-shirt that was worn by a man sharing fewer MHC alleles with them, also reported that the odor reminded them of a former partner, suggesting that preference shifts had influenced their actual mate choice in the past (Wedekind and Füri 1997). More recent research indicates that this phenomenon is found in some populations (e.g., Asian women), but not others (Jacob et al. 2002).

The Present Research

The literature reviewed above suggests that the shift in women's mate preferences, which occurs because of contraceptive pill use, adversely affects their offspring's immune system's adaptability. Specifically, it may impair mate selection processes and prevent beneficial gene coupling in future generations, resulting in extensive losses in the immune-system-parasite arms race. Although findings are reasonably congruent in suggesting that, at least in some populations, women's MHC preferences are reversed during pill consumption (Chaix et al. 2008; Roberts et al. 2008), research has yet to uncover the effects of pill consumption on offspring's health. In the present research, we examined whether children born to couples who met during regular contraceptive pill use would display more symptoms associated with a weaker immune system (e.g., being infection-prone, needing more medical

care) in comparison with children whose parents met when the mother was not using contraceptive pills.

Method

Participants

One-hundred ninety-two women aged 22 to 48 ($M = 33.51$, SD = 5.21) were either approached in various locations (e.g., family health center, parks, bus stations) or contacted by means of social network (e.g., Facebook) and were invited to take part in a study investigating children's health. All participants reported being the biological mother of a child 1–8 years old. Sixty-one women reported that they met their children's father while using contraceptive pill, whereas 119 women reported that they were not using contraceptive pill while they met their children's father. Sample size was predetermined by a power analysis (Faul et al. 2009) to achieve 80% power in detecting weak-to-moderate effects (4% explained variance) using analyses of covariance (ANCOVA; our main analyses). The analysis indicated that at least 191 participants are needed. Accordingly, our data-collection stopping rule was to have 191 participants who are eligible for the study.

Measures

Relationship and Contraception (RAC) Six items gathered information regarding medication consumption and the relationship status with the child's biological father during relationship formation. Three items (the first was dichotomous, and the others were open-ended) assessed current medication and contraceptive pill consumption ("Are you currently using contraceptive pills?"; "If you are using other forms of contraception, except for condoms, please specify which one"; "Do you take any medication regularly? If so, please specify which one"). Another dichotomous item inquired about the current relationship status with the child's biological father ("Are you currently in a romantic relationship with your child's biological father?"). The last two items (the first was dichotomous and the second was open-ended) assessed contraceptive pill or other contraceptive methods use during relationship formation ("Were you taking contraceptive pills when you met your child's biological father?"; "Were you using any other method of contraception other than pills and/or condoms when you met your child's biological father? If so, please specify which one").

Child Health Questionnaire (CHQ) This 23-item questionnaire (see Appendix) assessed two major aspects of child health. The first, Direct Health, which is the parental version of self-rated health, one of the strongest health predictors (Idler and Benyamini 1997), assessed the child's health directly (e.g., "How would you describe your child's overall health?"). Participants were also asked to rate their children's tendency to get sick, their overall health, overall relative health (in comparison with other children their age), child's relative speed of recovery when sick, number of visits to a medical institute to receive medical treatment, and number of hospitalizations, which are all perceived indicators of immunocompetence. The second, Indirect Health, measured additional health-related aspects, such as child's allergies, which are among the most common children's illnesses, whether or not the child was breast-fed, and whether the child is attending kindergarten or homeschool.

Some items (in both parts of the questionnaire) were phrased objectively (e.g., "How would you rate the overall health of your child?"), while others were phrased relative to other same-aged children in an attempt to minimize biased assessment (e.g., "How would you rate your child's health in comparison to other children of the same age?"). One item had multiple choices. The rest of the items were dichotomous, open-ended, or rated on a 7-point Likert scale ranging from *not at all/weak health (1)* to *very often/excellent health (7)*, respectively. For each participant, we calculated the following health-related scores: frequency of common illnesses (a compound measure of various illnesses, such as cold, stomach ache, and sore throat), infection proneness, perceived health, sickness frequency, perceived health in comparison with peers, perceived recovery in comparison with peers, and number of doctor visits in the last 3 months and in the last year.

Next, we conducted a factor analysis with maximum likelihood extraction method and direct oblimin rotation to assess the factor structure of these health indicators. The analysis revealed one strong factor (eigenvalue of 4.27) on which all of the health indicators are strongly loaded: frequency of common illnesses (0.63), infection proneness (0.72), perceived health (0.79), sickness frequency (0.77), perceived health in comparison with peers (0.84), perceived recovery in comparison with peers (0.64), and number of doctor visits in the last 3 months (0.53) and in the last year (0.49). Using Anderson-Rubin method, we calculated for each participant an overall health indicator with a mean of 0, such that positive values indicate poor health and negative values indicate good health.

Socio-Demographic Questionnaire We used a standard form inquiring about household income, religious inclination, education, relationship status, and children age and gender.

Procedure

The participants were asked whether they were the biological mother of a child between ages 1 and 8 years. This age range was selected because children in their early years are frequent users of health services (Hay et al. 2005). Women who failed to meet these criteria (e.g., were not mothers, were not the biological mothers of the child in question, or that their children were not within the needed age range) did not take part in the study and were thanked for their willingness to participate. Upon receiving a positive answer, participants were informed that 1000 NIS (roughly 260 US dollars) would be randomly awarded to one of the participants and that they were about to complete a packet of questionnaires for which instructions would be given. The participants were given an iPhone 4S containing an offline version of a Qualtrics (Qualtrics, Provo, UT, USA) questionnaire. In accordance with the instructions, the participants were reminded that they should have more than one child within the age range, and they should choose one and answer all child-related questions referring to him or her. The participants were given two trial questions to make sure they knew how to operate the phone and submit their answers. Upon completion of the questionnaires, the participants were given a lottery receipt and were thanked for their participation.

Results

To examine whether children born to couples who met during regular contraceptive pill use would display poorer health in comparison with children whose parents met under natural non-pill circumstances, we conducted an analysis of covariance (ANCOVA). Contraceptive pill use during the formation of the relationships (yes, no) served as the independent measure; children's overall health indicator served as the dependent measure. Given that family socio-economic status (SES) may affect the health care given to children (e.g., Adler and Ostrove 1999) and that maternal age may affect children health (e.g., Jacobsson et al. 2004), these variables served as covariates (SES and maternal age were not related to contraceptive pill use; see Miller and Chapman 2001). As predicted, children born to couples who met during regular contraceptive pill use had poorer overall health ($M = 0.21$, $SD = 1.20$) than children whose parents met under natural non-pill circumstances ($M = -0.14$, $SD = 0.85$), $F_{(1,\ 188)} = 4.50$, $p = 0.036$, $\eta^2_p = 0.03$.

To examine more in depth whether children born to couples who met during regular contraceptive pill use would display more symptoms associated with a weaker immune system in comparison with children whose parents met under natural non-pill circumstances, we conducted a multivariate analysis of covariance (MANCOVA). Contraceptive pill use during the formation of the relationships (yes, no) served as the independent measure; children's health-related measures (frequency of common illnesses, infection proneness, perceived health, sickness frequency, perceived health in comparison to peers, perceived recovery in comparison to peers, and doctor visits in the last 3 months and in the last year) served as the dependent measures; SES and maternal age served as covariates. Means, standard deviations, univariate test statistics, and effect sizes are presented in Table 1. Standard deviations were estimated by bias-corrected bootstrap analyses with 1000 resampling.

The analyses indicated that in line with the predictions, children born to couples who met during regular contraceptive pill use had higher infection proneness, weaker perceived health in comparison with peers, more doctor visits in the last 3 months and in the last year, marginally significantly higher frequency of common illnesses, and marginally significantly higher sickness frequency than children whose parents met under natural non-pill circumstances. There were no significant differences in perceived health and perceived duration of recovery from illnesses in comparison with peers (although results were consistent with the overall trend). Overall, the analysis explained between 2.4 and 7.8% of the health indicators' variance.

To examine whether these differences in contraceptive pill use could be linked with breastfeeding in infancy or exposure to other children in the education environment (home school, kindergarten), we conducted a series of Chi-square analyses for independence of measures using exact statistics (to account for any violations of basic assumptions). The analyses indicated that contraceptive pill use was not significantly linked with any of these measures: $\chi^2_{(1)} = 0.40$, $p_{exact} = 0.64$ for breastfeeding, and $\chi^2_{(1)} = 2.02$, $p_{exact} = 0.19$ for education environment. Interestingly, Chi-square analyses for independence of measures also revealed that contraceptive pill use was linked with the stability (or the lack thereof) of the relationship between children's parents, $\chi^2_{(1)} = 4.35$, $p_{exact} = 0.05$, such that 11.5% of the couples who met during regular contraceptive pill use got divorced as compared with 3.5% of the couples who met under natural non-pill circumstances.

Discussion

Democritus, the Greek pre-Socratic philosopher, has contended that "raising children is an uncertain thing; success is reached only after a life of battle and worry."

Table 1 Means, standard deviations, test statistics and effect sizes for contraceptive pill groups in health-related measures

	Users of contraceptive pill		Non-users of contraceptive pill		$F_{(1, 174)}$	η^2_p
	M	SD	*M*	SD		
Frequency of common illnesses	1.78	1.73	1.31	1.44	3.46~	0.02
Infection proneness	3.57	1.69	3.03	1.43	4.52*	0.03
Perceived health	5.53	1.50	5.86	1.07	2.34	0.01
Sickness frequency	3.35	1.42	2.96	1.12	3.23~	0.02
Perceived health in comparison to peers	5.13	1.54	5.55	1.06	3.98*	0.02
Perceived recovery in comparison to peers	4.80	1.45	5.00	1.30	0.78	0.01
Doctor visits in the last 3 months	1.87	2.39	1.25	1.41	4.12*	0.03
Doctor visits in the last year	5.71	7.36	3.99	3.73	3.75*	0.02

~ $p < 0.06$

*$p < 0.05$

As he noted, people tend to invest precious resources and the best of their years to secure their children's future. The present study, however, indicates that a key factor in achieving this goal might be traced to a choice people made years before their children were born: the decision to use a contraceptive pill. Our findings show that children of women who were on the pill during relationship onset are more often reported by their mothers to be infection-prone and require medical care, suffer from a higher frequency of common sicknesses, and are perceived as generally less healthy than their peers as compared with children of women who were not on contraceptive pill during relationship onset.

It is important to note, however, that although the present research does link children's weaker immune system with contraceptive pill use, it does not link this adverse effect with parents' MHC overlapping. To ascertain that these effects pertain to MHC-related mechanism, future research should examine the genetic profiles of parents based on contraceptive pill use at the onset of relationship. In addition, because of ethical considerations, the design of the present research is correlational (i.e., parents were not allocated randomly to contraceptive pill use conditions) and thus precludes conclusions regarding a causal link between contraceptive pill use and health. It is possible, for example, that a third unobserved measure (e.g., health status or certain personality characteristics of the women) might be the cause of both a higher likelihood of hormonal contraceptives use and noticing, recalling, or emphasizing a child's health problems. Animal models and longitudinal studies may thus be needed to carefully entangle this matter and appraise whether contraceptive pill use at the onset of relationship is the cause for offspring's poor health. Finally, in the present study, we asked women about contraceptive pill use but not about the exact type and dosage. Hence, we were unable to examine whether dosage rather than contraceptive pill use per se predicts children's health. Future studies should address this possibility as well.

Bearing the limitations of the present research in mind, the implications of our findings are profound as the use of contraceptive pills is widespread and still growing. Sixty-two percent of all US women in their reproductive ages are currently using a contraceptive method (J. Jones et al. 2012). The younger the woman, the higher the chances of using pills for contraception (54% of women using contraception under the age of 20 in the USA were on pills compared with only 11% of women between ages 40 and 44; J. Jones et al. 2012). The aftermath of these numbers is gloomy: the immune system of current-generation children might be more fragile than that of our ancestors, leaving the current and future generations more susceptible to pathogens and more dependent on medical care as its effective line of defense.

To date, antibiotics serve as virtually the sole ammunition of the medical age to treat bacterial infections when the immune system fails to hold the barricades. Recently, however, the World Health Organization (WHO) has issued the following alarming warning: "Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms emerge and spread globally every day, threatening our ability to treat common infectious diseases. A growing list of infections—such as pneumonia, tuberculosis, blood poisoning, and gonorrhea—are becoming harder, and sometimes impossible, to treat as antibiotics become less effective. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill. Tackling antibiotic resistance is a high priority for WHO" (WHO 2015). It seems, therefore, that an action should be taken so that our findings would not echo the words of T. S. Eliot, "This is the way the world ends; Not with a bang but a whimper." (*The Hollow Men*, 1925).

Appendix: Child Health Questionnaire

1. Does your child contract diseases easily?

1	2	3	4	5	6	7
Not at all						Very easily

2. How would you generally define your child's health?

1	2	3	4	5	6	7
Poor Health						Excellent health

3. How often is your child sick?

1	2	3	4	5	6	7
Not at all						Very often

	Not at all						Very often
4. How often does your child have a cold or a running nose?	1	2	3	4	5	6	7
5. How often does your child throw up?	1	2	3	4	5	6	7
6. How often does your child have a fever?	1	2	3	4	5	6	7
7. How often does your child have diarrhea?	1	2	3	4	5	6	7
8. How often does your child have a stomachache?	1	2	3	4	5	6	7
9. How often does your child have a sore throat?	1	2	3	4	5	6	7
10. How often does your child have a skin rash?	1	2	3	4	5	6	7

11. How would you define your child's health compared with other same-aged children?

1	2	3	4	5	6	7
Weaker Health						Better health

12. How well does your child heal compared with other same-aged children?

1	2	3	4	5	6	7
Faster than other children						Slower than other children

13. How many times has your child visited a medical institution for medical care in the last 3 months?
14. How many times has your child visited a medical institution for medical care in the past year?
15. Has your child ever been hospitalized due to an illness?
16. How many times has your child been hospitalized due to an illness?
17. Please specify the reason for the hospitalization: _____
18. Considering all hospitalizations, how many days in total did your child spend hospitalized?
19. Is your child drug-sensitive?
20. Does your child have allergies?
21. Was your child breast-fed?
22. Is your child still breast-fed?
23. Is your child currently attending nursery school or kindergarten?

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