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Mini Review Open Access

Medea Genes, Handedness and Other Traits

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Abstract

Medea factors or genes are maternal-effects mechanisms, found in many species, in which the mother's body selectively kills embryos of a certain genotype. Humans have a similar genetic mechanism, the gene *RHD* which produces Rh-factor involved in blood type. Recently I proposed that *RHD* acts as a maternal-effects gene that determines handedness (i.e., right handed or non-right handed) in individuals of our species. Here, I argue that *RHD* functions as a Medea gene as well. The handedness gene (and also *RHD* itself in some cases) has been implicated in autism spectrum disorders (ASD), bipolar disorder, cerebral laterality (i.e., right-brained or left-brained speech laterality), hair-whorl rotation, schizophrenia, sexual orientation, and speech dyslexia. Identifying the gene or genes that determine handedness or cerebral laterality may help uncover the mechanisms underlying these behavioral phenotypes in our species. A relatively simple test of the handedness hypothesis has been proposed: In a sample of humans for whom handedness has been evaluated, we would need to genotype for *RHD* by determining whether Rh+ individuals have one or two copies of the dominant allele. If *RHD* and perhaps also an interaction with *RHCE* are involved in sexual orientation, it explains how selection could favor a gene or genes which cause some people to become non-heterosexual.The literature on Medea genes provides the explanation: A Medea allele must increase in frequency, sometimes to fixation (i.e., 100% frequency) even if it reduces fecundity (e.g., birth rate). In addition, treatment for *RHD* maternal-fetal genotype incompatibility, which allows more fetuses to survive to term now, may be one explanation of why ASD appears to be increasing in frequency in some populations, if *RHD* is indeed the handedness gene, although many other mechanisms have also been suggested. One wonders if bipolar disorder and the other alternative phenotypes are also increasing in frequency.

Keywords: Autism spectrum disorders; Bipolar disorder; Cerebral laterality; Handedness; Maternal-effects gene; Medea gene; *RHCE; RHD;* Schizophrenia; Sexual orientation; Speech dyslexia; Speech laterality

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The literature on maternal-effects genes discusses a particular type of such genes, Medea genes, and a similar mechanism, the parasitic bacteria *Wolbachia* in insects, collectively known as selfish genetic elements because they represent a competition between the mother and father [1]. A Medea gene (and *Wolbachia* acts in a similar manner) is one in which the mother's body selectively kills embryos of a particular genotype, and such genes are known from plants, insects, and mammals [1,2].

Asymmetry in brain lateralization is a common trait among vertebrates, including mammals [3].Cerebral asymmetries are well documented in humans; in particular, handedness preference (i.e., right handed or non-right handed) and in the language-related areas of the brain (i.e., cerebral or speech laterality, right-brained or left-brained language dominance) [4]. Amar Klar [5] argued that the gene that determines handedness in humans is related to hair-whorl rotation (i.e., the direction the hair spins at the back of the head, either clockwise or counterclockwise), although this gene remains to be identified. Klar [6] showed that hair-whorl rotation was related to sexual orientation, Klar [7] implicated this same gene in schizophrenia and bipolar disorder, and other researchers showed that hair-whorl rotation was related to speech laterality [8]. Klar [5,6,7] also argued that the handedness gene is involved in speech laterality and may be involved in speech dyslexia. I argued that this gene (or these genes) may be involved in autism spectrum disorders (ASD) as well [9,10].

In those two previous papers [9,10], I proposed that *RHD*, the gene for Rh-factor, which determines whether one's blood type is Rh- (having no copy of the dominant allele) or Rh+ (having one or two copies of the dominant allele) acts as a maternal-effects gene that may be involved in handedness in humans. I also proposed that *RHCE*, another one of our *RH* genes, may be involved in cerebral (or speech) laterality, and an interaction between *RHD* and *RHCE* may be involved in sexual orientation and other behavioral phenotypes in our species, although this theory remains to be tested. It is relevant that *RHD* was recently found to be associated with sexual orientation [11]. They found that homosexuals were significantly more likely to be Rh-, as predicted by Hatfield [9]. However, other researchers [12] found no genes on chromosome 1, where *RHD* and *RHCE* reside, linked to male sexual orientation. However, they were not specifically looking for maternal-effects genes [10]. Similarly, no genes on chromosome 1 were found to be linked to handedness preference [13]. As with Sanders et al. [12], Armour et al. [13] were not searching for maternal-effects genes, although they were able to rule out two relatively simple genetic models.

Clearly, *RHD* operates like a Medea gene in our species because an Rh- mother's body can selectively kill Rh+ fetuses, especially male fetuses of higher birth order, if the mother is not treated for maternal-fetal genotype incompatibility during pregnancy. One elegant result that comes from the literature on Medea genes is that such an allele must increase in frequency, sometimes to fixation (i.e., 100%

frequency of the Medea allele), even if it reduces fecundity in a species [1]. For example, if *RHD* (or another Medea gene, for that matter) is involved in determining sexual orientation in our species, it explains how a gene that makes some people non-heterosexual could increase in frequency even though it reduces the birth rate of a population carrying such a gene or genes.

If *RHD* is Klar's handedness gene (which he calls *RGHT*), it would be relatively simple to test this hypothesis: One would need to genotype a sample of right handers and non-right handers and determine whether Rh+ individuals have one copy of the dominant allele or two copies (since Rh- individuals have no copies of the dominant allele). As I explained previously [10], if *RHD* is the handedness gene, it would function as a maternal-effects gene similar to the gene that determines shell chirality (i.e., either clockwise or counterclockwise rotation) in Gastropods (i.e., the alternative phenotype cannot be homozygous dominant, that is, having two copies of the dominant allele, see [14]). The snail chirality gene, in addition to the human handedness gene, *RGHT*, currently remains unidentified.

Furthermore, treatment for *RHD* maternal-fetal genotype incompatibility, which allows more fetuses to survive to term now, may be one explanation why ASD appears to be increasing in frequency if *RHD* is indeed the handedness gene, although many other mechanisms, both genetic and environmental, have also been suggested for the increase in prevalence [15]. Many of these children may not have survived in the past, but now most of them survive due to treatment of Rh- mothers for maternal-fetal genotype incompatibility to prevent death or harm to their Rh+ fetuses. Thus, if *RHD* is the handedness gene and as such is involved in ASD, then it gives another explanation why ASD appears to be increasing in some human populations. One wonders if the other alternative phenotypes (e.g., bipolar disorder) have also been increasing in frequency in our species.

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