Evolutionary approaches to autism: an overview and integration

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ABSTRACT: Autism is a highly heritable neurodevelopmental disorder, which greatly reduces reproductive success. The combination of high heritability and low reproductive success raises an evolutionary question: why was autism not eliminated by natural selection? We review different perspectives on the evolution of autism and propose an integration which emphasizes epistatic interactions between the effects of genes during development. It is well-established that autism is a polygenic disorder, and that the genes contributing to autism interact. If a disorder is polygenic, it is likely that the genes underlying the disorder are also involved in traits that are beneficial for the individual. For example, it is possible that genes involved in the development of autism are also involved in the development of intelligence. As intelligence is positively correlated with reproductive success, genes involved in autism can possibly spread in the population. We propose that in most individuals, the interactions between genes result in normal or high intelligence and the absence of autism. However, in some unlucky situations, often in combination with spontaneous negative mutations, the interactions between genes can lead to the development of autism (or other pathologies). Thus, the combination of high heritability and low reproductive success in autism can be explained from an evolutionary perspective that emphasizes the role of epistatic interactions in polygenic disorders.

Keywords: Autism, evolutionary psychology, heritability, epistasis

INTRODUCTION

Autism is a highly heritable neurodevelopmental disorder (1-2), with deleterious effects on reproductive success (3). The combination of high heritability and low reproductive success raises an evolutionary question (4): why was autism not eliminated by natural selection? In this paper we present an overview of theories that address the evolution of autism, and we formulate an integration of these different theories.

Autism as the result of an extreme male brain

The extreme male brain theory of autism postulates that affected individuals are extremely focused on systemizing as opposed to empathizing (5-6). Men, on average, appear to have a more systemizing brain than women, i.e., they are more interested in and better at analyzing variables in a system, and at deriving the rules that govern the behavior of a system. Women, on the other hand, seem to have a more empathizing brain, i.e., they are better at inferring mental states in other people, and to respond appropriately to these mental states. Empirical support for the extreme male brain theory of autism comes from several sources. First, more males are affected by autism than females (7). Second, high-functioning affected individuals (i.e., with an average or above average IQ) tend to outperform unaffected people with similar IQs on systematizing tasks (8). Third, the behavioral differences between people with and without autism are mediated by differences at the anatomical level of the brain (9). Fourth, prenatal exposure to testosterone (i.e., an androgen) is positively related to the development of autistic traits (10).

From an evolutionary point of view, in ancestral times, men with well-developed systematizing skills and under-developed empathizing skills may have had an advantage over other men (11). It is generally accepted that most humans used to live in hunter-gatherer societies, in which men fulfilled the role of hunter, and women the role of gatherer. Systematizing may have been important in developing tools and weapons, in hunting, tracking, and trading. Empathizing may have been disadvantageous in situations where rivals had to be eliminated, and in situations where one had to tolerate solitude, while being far away from home for hunting. Women, empathizing may have been more important because of mothering, making new friends (women used to marry into new groups), gossiping, and inferring the thoughts of a possible mate (to discover whether he is willing to invest in offspring). So having an extreme male brain, a condition which we strongly associate with autism, may have had practical advantages given demands of ancestral times. These advantages would have conferred greater reproductive success, thus ensuring the continued existence of this condition.

Autism as the result of an extreme imprinted brain

A second theory on the evolution of autism is the imbalanced genomic imprinting theory (12). Genomic imprinting refers to the expression of genes from only one of the two parental chromosomes (13). We inherit two copies of every allele, a maternal and a paternal copy. In most cases both copies are functional, but in some exceptional cases one of the factors is turned off (i.e., silenced) and is thus not functional. This may be the consequence of imprinting: maternal imprinting ensures that only the maternal copy is expressed, and paternal imprinting ensures that only the paternal copy is expressed. Imprinted genes show ‘parent-of-origin effects’ in the inheritance of traits: maternally expressed genes are inherited down the matriline, whereas paternally expressed genes are inherited down the patriline. The evolutionary function of imprinted genes is unknown. It has been suggested that genomic imprinting occurs between the sexes about the amount of investment of the mother in the child (14). Paternally expressed imprinted genes tend to promote fetal growth, whereas maternally expressed imprinted genes tend to suppress fetal growth. From the father’s point of view, it is beneficial that the mother invests as much as possible in the child. From the mother’s point of view, it is important to preserve her resources. This implies that it is beneficial for her to invest in the child only as much as is necessary.

It has been shown that imprinted genes are highly expressive in the central nervous system, and that they are involved in neurodevelopment (15). There is some evidence that maternally imprinted genes are expressed in the cerebral cortex and hippocampal regions, brain areas involved in cognitive processing, whereas paternally imprinted genes are expressed in the hypothalamus and septal brain areas (16), brain areas involved in emotional processing; however, this finding has not been replicated (17). Imprinted genes are often implicated in disorders, because a single change can dysregulate their function (18-19). Genomic imprinting has been linked to several disorders, including autism. Crespi and Badcock hypothesized that autism reflects reduced maternal brain functions, and enhanced paternal brain functions (12). This hypothesis is supported by the sex ratio in autism: more males are affected than females (7). A second source of evidence is provided by genome scans, which show that many of the genes involved in autism contain imprinted genes or genes that interact with imprinted genes (12).

Crespi and Badcock suggested that autism is the low-fitness extreme of a condition that is beneficial for the father (20). Children with autism impose additional demands compared to normal children, especially on mothers, who tend to be the primary caregiver. These demands include dealing with tantrums, attending to other people’s cooperative behavior, and lack of empathy. Normal children who display such behavior also impose additional demands on the mother, which is beneficial from the printing perspective, because the mother will spend more of her time and resources on the child. However, in the case of autism, the behavior of the child causes pathological proportions which no longer benefit either the mother or the father.
Autism as a low-fitness extreme of a parentally selected fitness indicator

A third theory postulates that autism is the low-fitness extreme of a parentally selected fitness indicator (21). A fitness indicator is a trait that takes conscious control to develop, maintain, and display. This cost makes it a reliable indicator of fitness, because the energy demands ensure that the indicator characterizes mainly the individuals who are capable of them. The peacock’s tail is a famous example of a fitness indicator that does not contribute to survival, but does help to attract mates. The peacock’s tail is a sexually selected trait. It is likely that there are also parentally selected fitness indicators; parents are likely to invest more of their resources in offspring that are more likely to survive and reproduce. Thus, it is possible that parential selection resulted in offspring traits that evoked parental solicitations. Photographs of autism show signals of weaning (22), and that autism is correlated with early weaning (23).

It is thought that evolution by natural selection is driven by the costs and benefits to the individual, as well as the indirect costs and benefits to the fitness of others. The main driving force behind the evolution of traits is the frequency of traits in the population. This can be calculated by the following equation:

\[ \text{fitness} = \frac{\text{fitness}_1 + \text{fitness}_2}{2} \]

Where fitness is the average fitness of two traits, and the fitness of traits is calculated by the following equation:

\[ \text{fitness} = \frac{\text{fitness}_1 + \text{fitness}_2}{2} \]

Each theory described above has its merit; each explains some part of the phenotype of autism and related traits, as well as their empirical evidence. It is possible to integrate these theories to arrive at a sensible account for maintaining and sustaining complex brain systems as well, therefore would not display the charming behaviors (at least not to the normal observers) that are reared in a favorable environment would be able to develop the complex brain systems required for high-quality behavior. Infants that are characterized by low genetic quality (i.e., a low mutation load) and that are reared in a favorable environment would be able to develop the complex brain systems as well, therefore would not display the charming behaviors (at least not to the same degree). In a few, the behavioral deviations would be so severe that we would associate them with autism. Evidence for this theory is that infants develop charm at the time when mothers start to show signs of weaning (22), and that autism is correlated with early weaning (23).

Autism as the result of a reptile brain

This perspective on the evolution of autism is provided by the Polyvagal theory (24). Polyvagal theory postulates that through three stages of phylogeny, mammals, especially primates, inducted an extension of a functional neural organization that regulates emotions and social behavior. The vagus, i.e., the 10th cranial nerve is a major component of the autonomic nervous system, which plays an important role in regulating emotions and social behavior. The three stages of phylogeny reflect the emergence of three distinct parts of the autonomic nervous system, each with a different behavioral function. In the first evolutionary stage, the parasympathetic nervous system evolved a functional neural network that regulates mobilization for death feigning and passive avoidance. These are typical responses to dangerous situations in reptiles, but atypical in mammals, including humans. In the second stage, the sympathetic-adrenal system emerged, which is characterized by mobilization as a response to dangerous situations. In the third evolutionary stage, the myelinated vagus emerged, which is involved in social communication, self-soothing and calming. It is proposed that people with autism minimize the expression of the mammalian response, i.e., social communication. Rather, they rely on the defensive strategies that include both mobilization and immobilization.

While normally primates and humans have a well-developed ability to shift adaptively between mobilization and social engagement behaviors, individuals with autism lack this ability. The resulting behavioral features lead to adaptive benefits in focusing on objects, while minimizing the potentially dangerous interactions with people. Without a readily accessible social engagement system, the myelinated vagus is unable to efficiently inhibit an autonomic state and is poised for flight and fight behaviors with the functional outcomes of frequently observed emotional outbursts or tantrums. The combination of a nervous system that favors defensive behaviors, and the inability to use social communication with people, places the autistic individual outside the realm of normal social interaction. Thus, due to the inability to engage the myelinated vagus to calm and dampen the defensive system (through social interactions), the nervous system of the autistic individual is in a constant state of hypervigilance or shutdown. These are generally adaptive responses in reptiles, but are severely maladaptive in mammals.

Towards an integration of different approaches on the evolution of autism: Autism as the result of epistatic interactions between the effects of genes

Each theory described above has its merit; each explains some part of the phenotype of autism and related traits, as well as their empirical evidence. It is possible to integrate these theories to arrive at a sensible account for maintaining and sustaining complex brain systems as well, therefore would not display the charming behaviors (at least not to the normal observers) that are reared in a favorable environment would be able to develop the complex brain systems required for highly charming behavior. Infants that are characterized by high genetic quality (i.e., a low mutation load) and that are reared in a favorable environment would be able to develop these complex brain systems as well, therefore would not display the charming behaviors (at least not to the same degree). In a few, the behavioral deviations would be so severe that we would associate them with autism. Evidence for this theory is that infants develop charm at the time when mothers start to show signs of weaning (22), and that autism is correlated with early weaning (23).

Assortative mating refers to the tendency of mat- ing with individuals who are phenotypically similar. It was found that mothers and fathers of children with Asperger syndrome, one of the autism spectrum disorders, scored highly on the Embedded Figures test, a test that is often included in IQ batteries (40). Both mothers and fathers of children with Asperger syndrome tend to have jobs that require high intelligence (41). Other studies revealed a positive correlation between the score of fathers and mothers of children with autism on measures of autistic traits (42-43), although another study did not confirm this (2).

A third piece of evidence for the involvement of epistatic interactions between genes in autism is the co-occurrence of autism and several other disabilities. There is ample evidence that autism co-occurs with medical syndromes (44), and minor physical anomalies (45). There is also considerable comorbidity with other psychiatric conditions (46). In addition, epistatic interactions between the effects of genes can explain the diverse array of phenotypes associated with autism spectrum disorders: in people with severe autism, which often co-occurs with mental retardation and physical disabilities, the effects of interactions between genes are extremely unlucky and most likely co-occur with spontaneous mutations.

The proposal that the combination of high heritability and low fertility in autism can be explained by the effects of epistatic interactions between genes that are involved in both intelligence and autism. However, some unlucky interactions, especially in combination with negative spontaneous mutations (30-31), lead to the development of autism, low intelligence, or other pathologies. With regard to autism, the unlucky effects of interactions between genes are negatively correlated to survival (32) and reproductive success (3). However, most of the time, interactions between the 30 genes lead to higher fitness (because of higher intelligence), and consequently, genes involved in autism can be beneficial. Thus, the combination of high heritability and low fertility in autism can be explained from an evolutionary developmental perspective that emphasizes the role of epistatic interactions in polygenic disorders.

There are several lines of evidence that support this idea. The first line concerns the relation between autism and intelligence or other exceptional abilities. A behavioral genetic study showed that there is substantial overlap between genetic factors that influence individual differences in autistic traits and intelligence (33). In addition, in autistic individuals, individuals with autism show equal or better performance levels compared to normal individuals. These tests include the Raven’s Progressive Matrices test (34) and the block design test (35). There is also evidence for the relation between autism and exceptional abilities, with some famous examples of autistic savants (36-37). The co-occurrence of savant syndrome and autism is an example of the interaction of epistatic interactions between genes, in which potentially beneficial effects of genes are nullified by the negative effect of autism, mental retardation, or other disabilities, on reproductive success (38).

The second line of evidence is the relation between assortative mating and autism (39). Autism prediction refers to the tendency of mating with individuals who are phenotypically similar. It was found that mothers and fathers of children with Asperger syndrome, one of the autism spectrum disorders, scored highly on the Embedded Figures test, a test that is often included in IQ batteries (40). Both mothers and fathers of children with Asperger syndrome tend to have jobs that require high intelligence (41). Other studies revealed a positive correlation between the score of fathers and mothers of children with autism on measures of autistic traits (42-43), although another study did not confirm this (2).
logical level, and this can be explained from a phylogenetic point of view. It does not explain the genetic background and the heritability of autism, so the reptile brain theory needs some extension to give a full explanation of the evolution of autism. The theory is not in disagreement with the idea that autism is the result of epistatic interactions between the effects of genes, so combining the two ideas may lead to a more complete account of the evolution of autism.

To sum up, this paper proposed a new theory that may explain the evolution of autism, which is a puzzle because of the combination of high heritability and low reproductive success. Epistatic interactions between potentially beneficial effects of genes may lead to unlucky gene expression that eventually leads to the development of autism. Earlier theories on the evolution of autism are not necessarily in disagreement with this new theory, but the new theory may serve as an integrative framework for different views on the evolution of autism.

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