

OPINION, VIEWPOINT

Autism may arise from brain's response to early disturbances

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From the perspective of basic biology, the syndrome of autism presents some major puzzles. For example, we know that multiple genetic, molecular and neuronal pathways are associated with its development, and that these can differ from one individual to the next. Yet to a skilled clinician, the key behavioral symptoms of the syndrome are clear, raising the question of how different pathways can lead to the same general outcome.

Although autism involves atypical development, I don't believe that we should refer to it as a 'developmental disorder.' In fact, it is a well-ordered developmental course that follows an unusual starting point. What are the implications of this view for current studies of autism?

Some researchers have aimed to find common elements in the molecular pathways regulated by the many different genes associated with autism¹. I have an alternative interpretation: In my view, the key behavioral symptoms of autism result from a common adaptive response by the brain to any one of a range of different disturbances around the time of birth.

To draw an analogy from physical illness, an increase in body temperature is a common systemic response that helps us combat a variety of widely different alien attacks, both bacterial and viral. Although the factors triggering a **fever** can vary enormously in their biological or environmental origins, they elicit the same adaptive reaction, which can eventually alleviate the illness².

Still, fever has negative side effects, and challenges to the immune system early in development can have lifelong consequences. Viewing autism in this light lets us address how an adaptive response by the brain to different genetic and molecular pathways gives rise to what is in fact a single syndrome.

Adaptive responses:

Much research in recent years has investigated how the human brain adapts to early genetic or environmental adversity, but these studies have mainly focused on brain mechanisms and cognitive strategies that help normalize behavior.

For example, some people with prosopagnosia, an inability to recognize individuals by their face, develop the ability to identify people by using other cues. As a result, the responses they present may seem typical to people who know them.

But adaptive processes during development do not always lead to a typical developmental trajectory. In a theoretical paper published earlier this year, my colleagues **Teodora Gliga**, **Emily Jones** and I proposed that self-regulatory operations help the brain adapt to subtle differences in the fidelity of processing at neuronal junctions called **synapses**³.

For example, in a process called 'niche construction,' an individual chooses to interact with the aspects of his environment that best fit how his particular brain processes information. Different kinds of disturbances to the efficiency of synapses can evoke the same responses from the brain as a whole, setting it on a developmental path that later results in the behavioral patterns characteristic of autism.

Another aspect of autism that needs to be explained is that both genetic and environmental factors can be important. For example, although autism is strongly associated with some disorders of

known genetic cause, such as **fragile X syndrome**, high rates of autism traits are also common in children raised in impoverished early settings, such as **Romanian orphanages**.

We can address this issue by considering the ‘perceived environment’ — that is, the environment as processed by the brain — as the guide to adaptation. Even subtle brain differences early in life mean that different brains sample the same environment in different ways. In other words, the environment as experienced by the atypical brain is different, and it is this perceived environment that it adapts to over its developmental course.

In other cases, such as the Romanian orphanages, the brains of children may not differ significantly from typical, but the environment does, triggering the same whole brain adaptations.

Building on these points, I suggest that the main behavioral features of autism at the time of diagnosis reflect earlier processes of whole-brain adaptation, and so are not necessarily the direct products of an ongoing brain pathology.

For example, withdrawal from the social world may be a sensible adaptive response for a person whose brain early in life had trouble processing interactions with others. And once set upon this path of development, reversing it to restore typical behavior may be hard.

In the same way, an overly narrow focus of attention is a perfect adaptive strategy for a brain that has difficulty computing large quantities of information. By focusing on specific objects, or domains of interest, an atypical brain can tune in to a comprehensible subset of the world. Again, once set on this course, the brain later in life may not be flexible enough to widen its focus, even if the original underlying factors dissipate.

One area of research that I believe merits a new interpretation involves functional and structural brain imaging studies on adults diagnosed with autism. Typically, when researchers present results that show differences from neurotypical individuals, they interpret them as evidence of an underlying and continuing pathology.

I argue that these investigations essentially reveal the brain’s adaptations to differences that occurred earlier in development. It is sobering to reflect that such studies of brain structure and function in autism may not, in fact, inform us about the primary causes of the condition.

Another implication of our view is that researchers studying early interventions for autism will need to consider carefully whether an attempt to shift behavior or brain processes toward typical function (‘normalization’) is the most appropriate goal for an individual with autism.

One critical objective may be to identify whether the non-optimal synaptic function that triggered the adaptive process is still present at the time of intervention, or whether the original underlying problem was transient and has now resolved. If we can focus on determining the function of the

adaptations at different stages of development, we will be better able to tailor interventions to individuals.

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References:

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