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## Risk factors:

Baby steps towards understanding the development of autism.

By SCOTT HUBERTY

In a previous issue of Sur Le Spectre, a geneticist explained that hundreds of genes appear to be associated with autism. They also paint a more complex picture, pointing out that many of these genes are also linked to other developmental conditions and people without a diagnosis, and may impact individuals differently. This article takes the discussion a step forward discussing the array of biological and non-biological factors leading to autism diagnosis and other behavioural outcomes.



Original Reference: https://plos.figshare.com/articles/ figure/\_Waddington\_s\_8220\_Epigenetic\_Landscape\_8221\_/620879

or a developmental condition (risk factors), and a person's actual developmental outcomes, as a landscape: In the picture below, the ball at the top of the hill would represent an infant, and the hill below represents different potential developmental journeys. The presence of one or more risk factors that increase autistic likelihood can nudge an infant towards a certain developmental path. The start of each path represents early brain development, and further down the hill represents behavioural development. You may have noticed that it appears easier to switch between paths when higher up the hill; this reflects that earlier in life there is greater brain plasticity (the ability to amend connections between neurons).

In autism, researchers now have identified some risk factors that increase the likelihood of autism. The table below (Figure 2) presents some of the many factors that are recognized in the scientific community as being associated with autism (Part A). These factors are usually present from birth and are thought to influence the development of brain networks by shaping how neurons form connections with one another (Part B). This different brain development can in turn influence behavioural outcomes in domains either specific to autism (i.e. social communication) or more broadly (such as language development) (Part C).

It can be useful to conceptualize this relationship between factors that increase the likelihood of developing autism

However, these risk factors (part A), despite being consistently associated with higher likelihood of autism,

are also seen in other developmental conditions. That means they are not unique to autism, and more research needs to be done to better understand how two individuals with the same risk factors (both having the same genetic mutation for example) can diverge in two distinct developmental journeys.

		Pregnancy	0-12 months	12-24 months	24-36 months	
•	Risk Factors	Family history of ASD Family history of autoimmune disease Advanced parental age Maternal overweight Maternal infection	Birth injury or trauma Low birth weight Presence of an «clinically Genetic diagnosis such a Angelman, CHARGE, Fray 22q11.2 deletion.	significant» genetic mutation s : Rett, Cohen, Cornelia de La gile X, neurofibromatosis type 1	nge, Tuberous sclerosis, 1, Down, Noonan, Williams,	
8	Brain Development		Atypical development of t Enhanced perceptual skills	pical development of brain networks hanced perceptual lis Reduced flexibility in attention disengagement Diminished attention to social information		
G	velopment		Developmental delays, especially in language Troubles with sleeping / feeding Extremes in temperament Emergence of unusual play, sensory or repetitive behaviors			
0	dentification de			Diminished social commun	Diagnostic assessment	

Figure adapted from the original paper

Because changes in the brain typically precede changes in behaviour, studying early brain development in infants can help us to better understand how the aforementioned risk factors determine which developmental journey a child might follow. Most studies aim to do this by following infants who have an older autistic sibling, because family history of autism is a factor that increases the risk of developing autism.

These studies often record EEG (a non-invasive tool that measures the activity of brain networks, sometimes referred to as brain waves!) with the infants. By recording EEG at multiple time points throughout early development, researchers can gain a clearer picture of how the brain develops in children, and whether certain risk factors influence this brain development. A team led by Dr. Mayada Elsabbagh at McGill's is leading such a study that has collected EEG's from over 400 infants from both North America and Europe multiple times throughout the first years of life. By studying the relationship between risk factors of autism, brain development, and developmental outcomes, Dr. Elsabbagh and her team hope to help us better understand what determines the developmental journey a child will undergo, particularly in children at risk for autism.

## **Original Reference:**

Elsabbagh, M. (2020). Linking risk factors and outcomes in autism spectrum disorder: Is there evidence for resilience? British Medical Journal (Clinical Research Ed.), 368, I6880. https://doi.org/10.1136/ bmj.I6880