

Interview: Henry And Kamila Markram About The Intense World Theory For Autism

1. The Intense World Theory sheds light on the mystery of autism, and offers fascinating and refreshing insights. This theory may baffle those with a limited understanding of neuroscience. How would you explain Intense World Theory to the layman?

The Intense World Theory states that autism is the consequence of a supercharged brain that makes the world painfully intense and that the symptoms are largely because autistics are forced to develop strategies to actively avoid the intensity and pain. Autistics see, hear, feel, think, and remember too much, too deep, and process information too completely. The theory predicts that the autistic child is retreating into a controllable and predictable bubble to protect themselves from the intensity and pain. The theory originated from neuroscientific discoveries on an animal model of autism and was extended by accounting for previous research on autism in humans. It is a unifying theory because it takes into account and explains the many different results and interpretations from a spectrum of studies on autism.

The brain is supercharged because the elementary functional units of the brain are supercharged. These units are called neural microcircuits. Neural microcircuits are the smallest ecosystem of neurons that can support each other to carry out functions. The brain is made up of millions of these units. These microcircuits are hyper-reactive and hyper-plastic. That means that they react and process information much faster and more intensely, they can learn much more and remember much longer, and they can remember things with much greater detail. The Intense World Theory proposes that having such powerful units makes orchestration difficult – like trying to play a piano with a million run-a-way keys. The microcircuits that are mostly affected will depend on genetics, toxic insults during pregnancy and the kind of environmental exposure after birth. Each autistic child will therefore be unique because different microcircuits are hyper-functional and they dominate the idiosyncratic pattern that emerges.

The theory predicts that there are three factors in the cause of autism; a genetic predisposition, a toxic insult during pregnancy and environmental exposure after birth. Our genes normally switch on an off in a well-timed and precise sequence like the playing of a piece of music throughout life. Autism is a triggered acceleration of this cascade of gene expression during brain development. We believe toxins during pregnancy trigger this acceleration. Many possible genetic mutations can lower the threshold for triggering the accelerated cascade. Environmental exposure that normally accelerates brain development accelerates brain development even further in autistics making the brain too sensitive, too early.

The danger of accelerated brain development is that all the steps needed to complete the trimming down of the connections between neurons is not completed and that some microcircuits that should wait their turn to develop, develop too early and begin to dominate over the other microcircuits driving hyper-preferences, repetitiveness, idiosyncrasies and eventually making unlearning and rehabilitation very difficult.

While it will be difficult to reverse and correct these developmental changes completely, the theory points to many exciting new possibilities for diagnosing, treating and helping autistic children benefit from their unique brain. For example, if the environment can be carefully controlled after birth, then the autistic child could potentially keep the supercharged

microcircuits as well as their ability to orchestrate these microcircuits to fully express their genius without the suffering that can come with a supercharged brain.

2. Describe the evolution of Intense World Theory from inspiration to publication.

Our research into autism started in 1998 while Henry Markram was at the Weizmann Institute. Henry has an autistic child (now 16 years old) and was of course motivated to understand him. At that time most researchers were looking at the cerebellum, brain stem and other areas for alterations and very few were looking at neocortical alterations. Henry thought this was odd since most of the symptoms in autism are related to alterations in perception, attention and memory, and such advanced functions depend heavily on normal neocortical functions. In 2000 Henry went on sabbatical to Michael Merzenich lab at UCSF and proposed that perhaps the excitatory-inhibitory balance was affected. Henry first thought that inhibition was impaired and received a grant from NAAR (National Alliance of Autism Research) to establish how the inhibitory system is recruited in the normal brain and in animal models of autism.

This research continued when Henry moved to the Swiss Federal Institute for Technology in Lausanne (EPFL). His student Tania Rinaldi used the valproic animal model of autism, which seemed promising based on the work of Patricia Rodier. They could not find malfunctions in the inhibitory synapses and started looking at the excitatory connections. They found that too many excitatory connections were formed in the neocortex of autistic animals. They also found that the circuit responded much too strongly when stimulated and that the synapses learned much easier than normal about the stimulus.

Kamila Markram, a behavioral neuroscientist working in Carmen Sandi's laboratory, then stressed the importance of also examining the amygdala because autism has a profound emotional component and because previous theories suggest that the amygdala is malfunctioning, that it is hypo-functioning and that autists can't interpret people's feelings and have dampened down emotions. Kamila carried out behavioral studies on the animal model and found that the autistic animals developed excessive fear memories, that these fears lasted much longer and were difficult to undo. She also found that they generalized these memories too easily to associated stimuli (i.e. once afraid of a sound with a certain pitch, they become afraid of all sounds regardless of the pitch). Kamila realized that this could lead to autistic children quickly to becoming fearful of parts of the world for no apparent reason and it would make rehabilitation very difficult. This also suggested that one would need to be extremely careful when exposing an autistic child to the world and especially when punishing an autistic child. They will never forget the punishment and generalize it quickly to a point where they will fear so many things that they not be able to function normally. Kamila then re-examined all previous studies by all major laboratories that studied autism and reinterpreted their results in this new light.

Kamila and Henry then came up with a unifying theory that accounts for the facts and first called this the intense world syndrome hypothesis. Further experiments in their lab on how genes and proteins are expressed as well as an even deeper analysis of past studies culminated in the Intense World Theory.

3. Many members of the autistic community have embraced Intense World Theory, claiming it to be an accurate reflection of their own experiences, and a radical departure from the outdated and socially stigmatizing disease models of the past. Why has it taken so many years for the scientific community to draw a conclusion which autistics themselves find to be quite obvious? What prevented Intense World Theory from emerging years ago?

The main reason is that historically autism has been classified as a form of mental retardation. Biologically, mental retardation results from malfunctions in genes, proteins, cells, synapses and circuits and so most researchers were just looking for evidence of malfunctions because scientists mostly look for evidence to support current theories and hypotheses. Autism is still today classified as a form of mental retardation in the bible of brain diseases, the Diagnostic and Statistical Manual of Mental Disorders. This superficial classification has led to scientists looking for malfunction, hypofunction, and deficits at the biological level. So the research has become messy and confused and many mistakes have been made in the interpretation of experimental results.

The second major mistake is that scientists have reasoned that because every autistic child is so unique that there are many different causes of autism. The consequence has been that each researcher has made localized interpretations of their data and proposed their own isolated theory of autism ignoring “the other forms” effectively hiding behind “the spectrum”. We can see the result – today there are dozens of fragmented theories of autism that each focus on a specific aspect of autism.

The third major mistake has been the belief that autism is primarily a genetic disorder. There is of course good reason for this because the second twin of identical twins has a much higher chance of having autism than in the general population, but this has led researchers to hunt only for the genetic malfunction while ignoring the fact that the twin of an autistic child that has the “bad” gene(s) does not have autism – this also proves that autism can be cured if we understand it. The hunt for bad genes has also led researchers to play down toxins as triggers of autism and injected confusion when it comes to whether the incidence of autism is increasing. Together this has resulted in researchers ignoring how genes can lower the threshold for autism triggered by a toxin or to such a low level that the probability of that autism can be spontaneously triggered without a toxin, is significantly increased.

There are many other reasons such as strong prejudices in how autism must be studied. On the one hand, some believe that one can only study autism in humans. Humans are mammals and what makes us mammal special is the neocortex. The microcircuitry of the mammalian neocortex is very similar. There are small variations in each species, but far more is preserved than changed. It is therefore illogical to say that autism can only happen in humans. This assumes that some gene or protein only found in humans must be the cause of autism and there is no evidence of that. A related community has argued that since it is a human disorder the closest relative, the monkey must be used in the studies. This led to one of the biggest detours in autism research where the amygdala was lesioned in monkey. When the amygdala was destroyed in monkeys, they also withdrew and showed no emotionally driven behavior. Scientists then thought that this proves that autism is a disorder of hypofunction of the amygdala. This was a relic of the theory that autism stems from malfunctioning systems that started with the refrigerator-mother theory many decades ago. On the other hand, there is a community that believes that autism is genetic and the only relevant animal model is the mutated mouse. The problem with this line of research is that they mostly still look for malfunctions.

More recently, these studies have also started testing for hyperfunctions so it is a good sign that the Intense World Theory is starting to change the field. Since hundreds of genes can be involved in setting the threshold for autism, these studies will however have to go to the next level rather than try to prove one gene at a time. What is really needed is to understand how the gene expression cascade is altered starting as early as possible in development. Epigenetics and behavioral studies after birth will therefore become central to the research into autism in the future.

4. Intense World Theory has been widely accepted by supporters of the Neurodiversity movement. Were these sociological implications foreseen in early development, and if so, can their influence be found in the published text?

This was not a factor in the discovery of the Intense World Theory. The theory was triggered bottom up from neuroscientific studies and the real changing point for us was when we found that fear memories were so quickly acquired, lasted longer, were difficult to erase and overgeneralized. This put all the results into context because the neocortex could render the world intense, highly fragmented and overly specialized while the amygdala would dial up the emotional component of the intense world making it potentially extremely painful and aversive forcing the autistic child to take refuge in a secure bubble. If they don't succeed to take refuge through repetitive behavior, routines, rocking, and other types of behaviors, then they may display self-injurious behavior – like ants crawling all over your body. The diversity comes from the fact that we are normally diverse and if you add hyperfunctional circuits to that then naturally each autistic child will be even more different from each other. It is like taking all our normal differences to an extreme. This challenges society to accommodate autists, but diversity is the key to social evolution and so it is a good challenge.

5. How does the alternative cognitive style of the autistic mind prove beneficial or detrimental to autistic self-advocacy?

Autistics could be at the pioneering edge of human brain evolution. Society should embrace and support this exploration into the extraordinary. According to the Intense World Theory, if autism can be identified at birth, then a well-structured and filtered environment could allow the sequence of brain development to unfold normally while preserving the hyperfunctional microcircuits. This does not mean the environment must be impoverished, in fact it should be a rich and diverse environment, but presented in a gentle and predictable way. Great care should be taken since any surprising event could be traumatic and potentially trigger a cascade of development that is difficult to reverse. Behavioral treatments that apply strong negative and positive reinforcement could have serious adverse effects according to the Intense World Theory, especially at a very early age. Such treatments are better suited to mental retardation or to older autists that have passed through the critical phases of brain development. The idiosyncratic behavior of autistics should be respected as they can make a unique and highly valuable contribution to society. Autists should fight for the way they believe the next generation of autistic children should be raised – those that succeed to free their locked up genius can help free the next generation. Society should compensate and help families with autistic children.

6. Disregarding social and ethical implications, do you believe an autism cure is a scientific possibility? Why or why not?

The Intense World Theory predicts that all autistic children have exceptional talents that are locked up. The challenge is to free talents and to make it possible for them to integrate in society. We do believe that autism can be turned into a highly beneficial “disorder” if we understand how to help the autistic child harness their genius rather than suffer from it. The route is to understand the epigenetic alterations so that we can make better and earlier decisions on the direction of therapy. We also need to understand all the different ways that we can raise the threshold of epigenetic alterations so that the progression does not become so severe as to lead to a social handicap. We have to be prepared to develop a custom treatment for each autistic child. We have to be prepared to create special environments for the early stages of life of an autistic child. If this is all done, most autistic children could pass through the critical periods of brain development quite normally and emerge from it with their full genius intact.

7. Do you believe the direction of autism research must be dictated by a governing social conscience, or does such a conscience corrupt scientific objectivity?

A social conscience must always govern all kinds of scientific research not just for autism research. Scientists cannot just do anything in the name of science. It must always be justifiable at all levels of society and actually understandable to all people. Co-evolution of science and society makes for a healthy planet.

8. “Unraveling the Paradox of the Autistic Self,” by Michael V. Lombardo and Simon Baron-Cohen, states that “neural evidence provides a key clue that an ‘egocentric’ response in the brain (i.e., Self = Other) is actually the result of an impairment in self-referential coding of information.” Do you believe an elusive sense of self is a universal autistic characteristic? Does Intense World Theory account for this impairment?

Well, we would not agree with their analysis and theory. This is just another theory that is a relic of the theories of mental retardation. It is contaminated by older theories that there is a deficit in the ability of the brain to develop a theory of mind, the ability to see and respect others thoughts feelings and emotions. This archaic theory has also led to gross misinterpretations of the mirror neuron discoveries. According to the Intense World Theory, autists could actually be seeing much deeper into the minds, thoughts and emotions of themselves and others, which triggers active avoidance and lock down behaviors. It also requires the ability to simulate others as if you where them and to extrapolate to where their thoughts and behaviors are leading them. Seeing into the minds of others can be extremely disturbing. Even if autists don't feel this is true for themselves it is because their brain has developed strategies to cope with this extreme insight leaving them seemingly isolated.

This theory of a deficit in self-referential coding or theory of egocentricity is also likely to be incorrect for another reason. Self-referential coding is the foundation of human consciousness. To be conscious of yourself and others requires you to have to be able to localize yourself in space and time. If you enter an isolation tank, anesthesia, or deep meditation you can lose track of yourself, where you are, who you are, what time it is. So impairment in self-referential coding will also mean that autists are barely conscious and living in peaceful state of diffused consciousness (pain is based on a sense of self, locality). It is most likely the exact opposite of autists. They are in an extremely localized state, extremely aware of themselves, extremely aware of others and in a battle for their life to hold back the intensity and pain of it all.

9. Intense World Theory proposes that autism is “hyper-functioning of local neural microcircuits, best characterized by hyper-reactivity and hyper-plasticity.” Does this mean that savantism may be a universal, though not always objectively measurable, autistic characteristic?

Absolutely. In fact the Intense World Theory predicts that severely autistic people that cannot speak or interact at all have locked up abilities even greater than savants. In other words, those autists classified as severely mentally retarded by the psychiatrist, may be the greatest savants of all. Savants as we know them are just lucky that they retained the ability to express themselves. The Intense World Theory predicts that the amygdala is less affected in savantism so the pain of the intense world is dialed down making it easier for them to cope with what they see, hear, feel and think, and allowing them to express themselves. There is so much potential lying behind this wall of pain and fear.

10. Do you believe Intense World Theory will endure the test of time, and have a long-term scientific and sociological impact? Predict the legacy of Intense World Theory.

Scientific theories probably never last indefinitely. However, we do believe that the Intense World Theory will replace all existing theories because it is the only unifying theory of autism today. Other theories are piece-meal theories accounting of a selective set of observations and mostly based on a paradigm of autism as a form of mental retardation. Nobody likes one to come up with a unifying theory that explains all the facts. It will take time for scientists to embrace it and they will argue that it does not explain their corner of the facts because they like to interpret their facts in a certain way, they will use the fact that it is based on rodent brain changes to avoid the theory for as long as possible. The hyperfunctional theories such as those of Laurent Mottron have gone in the same direction. Rebellion and criticism is part of every scientific revolution where the paradigm is turned upside down.

The Intense World Theory predicts so many exciting completely new directions for autism research, for autistics, and for society that we believe this theory will last a long time.

For research, we will isolate various agents that can induce epigenetic insult of the genome and may even learn how to use these agents to guide evolution of the human brain. We will learn which sets of genes are predisposing – lower the threshold of epigenetic insult during pregnancy – so that we can be better informed on nutrition during pregnancy and get ready to raise an autistic child if necessary. We will learn how to gently guide the development of the brain of an autistic child through the critical irreversible periods and avoid traumatic moments that could spin the brain development into a nightmare configuration and preserve the hyperfunctional microcircuits allowing autists to cope with the intensity and pain and express their genius. Nutrients, drugs and other treatments such as brain stimulation, will emerge that can dampen down selectively some uncontrolled hyperfunctional components.

For autists, they will learn how to nurture rather than lockup the deep insight and how to contribute these insights to society. We will learn how to help the next generation of autists cope and express their individual genius.

For society, we will learn how valuable the autistic community is for society. We will adapt the planet to embrace rather than lockup autistic people. Normal people guess at the world, while autists process information completely, comprehensively. This feature would not be good for survival in the jungle, but in human society, we can nurture these individuals and they can make a fantastic contribution to society. We will begin special compensation to families with autistic children as if they are potential Olympic athletes of the world.