A review of theories of Autism Spectrum Disorder

Hassan Shahrokhi M.D.
(Child & Adolescent Psychiatrist)
Assistant Professor- TUoMS

Theory of Mind theory

- Strength
  - Social and communication difficulties in ASC
- Its shortcomings :
  - It cannot account for the non-social features
  - Ignore emotional component of empathy
  - Mindblindness may not be specific to ASC

Central Coherence Theory

- Limited ability to understand context or to "see the big picture”
  - Focus on local processing
- May be people with autism or AS start their cognitive processing by focussing in on the most local details
  - Local detail is simply the best (possibly the only) place to start.
  - Studies of autistic ‘savants’ show that there is often a good implicit understanding of the rules of the system

The Extreme Male Brain Theory

- An attempt to alleviate shortcomings of mindblindness theory
  - Excellent attention to detail
    - As a universal feature of the autistic brain

Empathizing

- **Empathizing**
  - Drive to identify another person's emotions and thoughts and to respond to these with an appropriate emotion
    - Empathising involves an imaginative leap in the dark, in the absence of much data
    - **<u>Female advantage in empathy</u>**

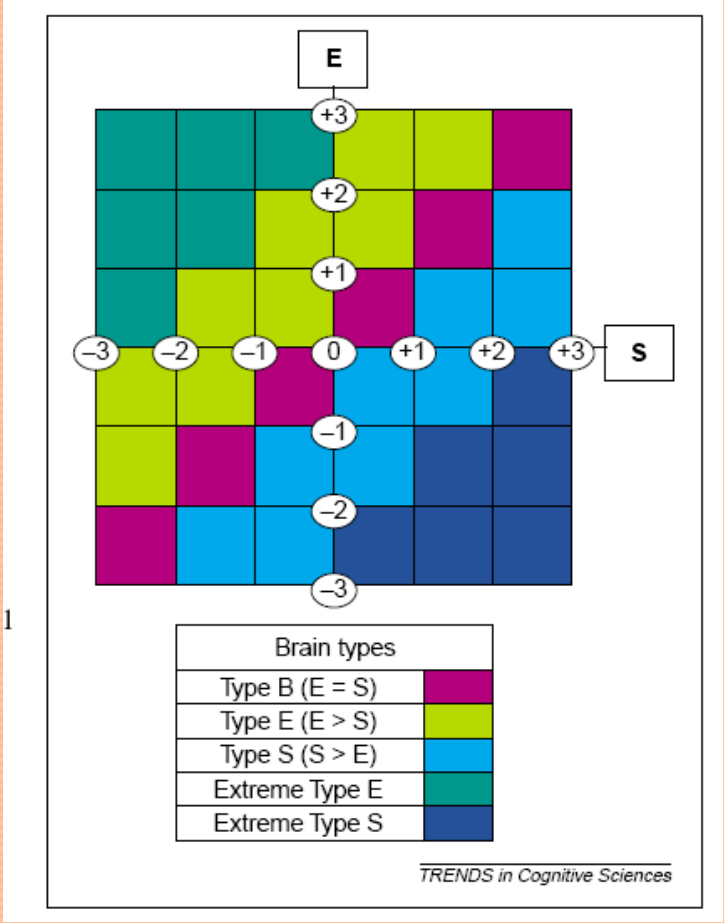
SYSTEMIZING

- Drive to analyse the variables in a system, to derive the underlying rules that govern the behaviour of a system.
- Male advantage of systematizing

Role of biology in empathizing and systematizing

- 1-day-old babies, boys look longer at a mechanical mobile than at a person's face
  - One-day-old girls show the opposite profile
- Amount of time a 1-year-old child maintains eye contact is inversely correlated to the level of foetal testosterone (FT)

The main brain types



Autism: Hypersystemizing alongside impaired empathizing?

- Neuroimaging during empathy tasks
  - Reduced blood flow in the amygdala and medial prefrontal cortex
- Fathers—and even grandfathers—of children with ASC are twice as likely to work in the occupation of engineering
- Students in the natural sciences (engineering, mathematics, physics) also have a higher number of relatives with autism
- Mathematicians have a higher rate of AS, and so do their siblings
- Both mothers and fathers of children with AS have been found to be strong in systemizing on the Embedded Figures Test
- Scientists score higher than nonscientists on the Autism Spectrum Quotient (AQ).
  - Mathematicians score highest of all scientists on the AQ

Autism: an extreme form of the male brain

- Autism spectrum conditions affect males far more often than females.
- Impaired empathising in ASD
- Superior systemising in ASD
- **Biological and familial evidence**
  - The Autism Spectrum Quotient (AQ).
  - Sexually dimorphic somatic markers.
  - Early puberty.
  - Familiality of talent.

Repetitive behaviour within the hypersystemizing theory

- Was traditionally described as “purposeless” and as a “symptom”, suggesting it lacks purpose or value.
- In fact, within the hypersystemizing theory, it has a very clear purpose:
  - To provide input for a neural mechanism whose sole function is to seek and find patterns in data.

Neurological evidences for The Extreme Male Brain Theory

- In regions of the brain that on average are smaller in males than in females people with autism have even smaller brain regions than typical males.
  - the anterior cingulate, superior temporal gyrus, prefrontal cortex, and thalamus
- In contrast, in regions of the brain that on average are bigger in males than in females, people with autism have even bigger brain regions than is typical.
  - the amygdala, cerebellum, overall brain size/ weight, and head circumference
    - Not all studies support this pattern but some do
- Consider fetal testosterone as one candidate for hyper-masculinization

Implications of The E–S theory for intervention

- "Systemizing empathy,"
  - Presenting emotions in an autism-friendly format
- Taking the quite artificial approach of presenting mental states (such as emotional expressions) as if they are lawful and systemizable, even if they are not

The Empathy Imbalance Hypothesis

- According to this account, people with autism have a deficit of cognitive empathy but a surfeit of emotional empathy.
  - The behavioral characteristics of autism might be generated by this imbalance and a susceptibility to empathic overarousal.

Empathy

- Cognitive Empathy (CE)
- Emotional Empathy (EE)
- *Emotional contagion ?*

Direct and indirect EE

- Direct :
  - Spontaneous EE not derived from CE
  - The empathizer may or may not be fully aware that he or she is sharing the emotion of another.
- Indirect EE
  - EE derived from CE

Autistics in light of EIH

- They would have a strong capacity for direct EE but a reduced capacity for indirect EE.
- Their sense of self would easily be permeated by other people's emotions and that this could be a confusing and aversive experience
- People with CE deficit disorder might particularly enjoy the company of happy people who behave in consistent and predictable ways.
- EE sensitivity is positively correlated with automatic mimicry of facial expressions

Neuroimaging research on gustatory empathy

- Anterior insula
- Involved in gustation when they observe other people's facial expressions of gustatory emotion
- Activation of the gustatory cortex appears to be positively correlated with an individual's susceptibility to emotional contagion and personal distress
- People with CE deficit disorder can be expected to show heightened neural responsiveness to the gustatory pleasure of others.

Autistic Behavior as an Adaptive Response to Empathic Imbalance

- People with autism may try to control and narrow their attention in an attempt to regulate EE.
- People with autism would be more willing to pay attention to calm, happy people than to distressed or angry people.
- Exuberant positive emotion in others may also sometimes cause confusion and an uncomfortable degree of empathic arousal in children with autism
- It is painful for them to make eye contact because of the emotional significance of the eyes
- Stereotypic patterns in autism might sometimes be an attempt to prevent or disengage from empathic connections.

Implications for therapy

- Emotional status of other people can be expected to influence the behavior of children with autism
- Displaying positive emotion in consistent and predictable ways could be one of the most therapeutic techniques that caregivers might employ.
- It might reduce the frequency of avoidant, stereotypic, or challenging behavior in people with autism

The Intense World Theory

- *Grounded in original experiments using the valproic acid (VPA) rat model of autism to explore possible alterations across molecular, cellular, synaptic, circuit, and behavioral levels.*
- VPA intake during pregnancy was linked to an increased risk of giving birth to an autistic child and VPA exposure in rats has remarkably similar effects
- The multi-level approach from molecules to behavior

The neurobiological basis of the Intense World theory

- The neocortex
- Somatosensory circuit in the rat
- The prefrontal cortex
- The amygdala

Hyper….

- **Hyper-Reactivity**
- **Hyper-connectivity**
- **Hyper-Plasticity**
- **Hyper-NMDA Receptor Expression (?)**
- **Hyper-Perception in Autistics**
- **Hyper-Attention in Autistics**
- **Hyper-Memory in Autistics**
- **Hyper Intellect in Autistics (?!)**
- **Hyper-Learning in VPA-exposed rat**
- **Hyper-Emotionality in Autistics**
- **Hyper-Fear**

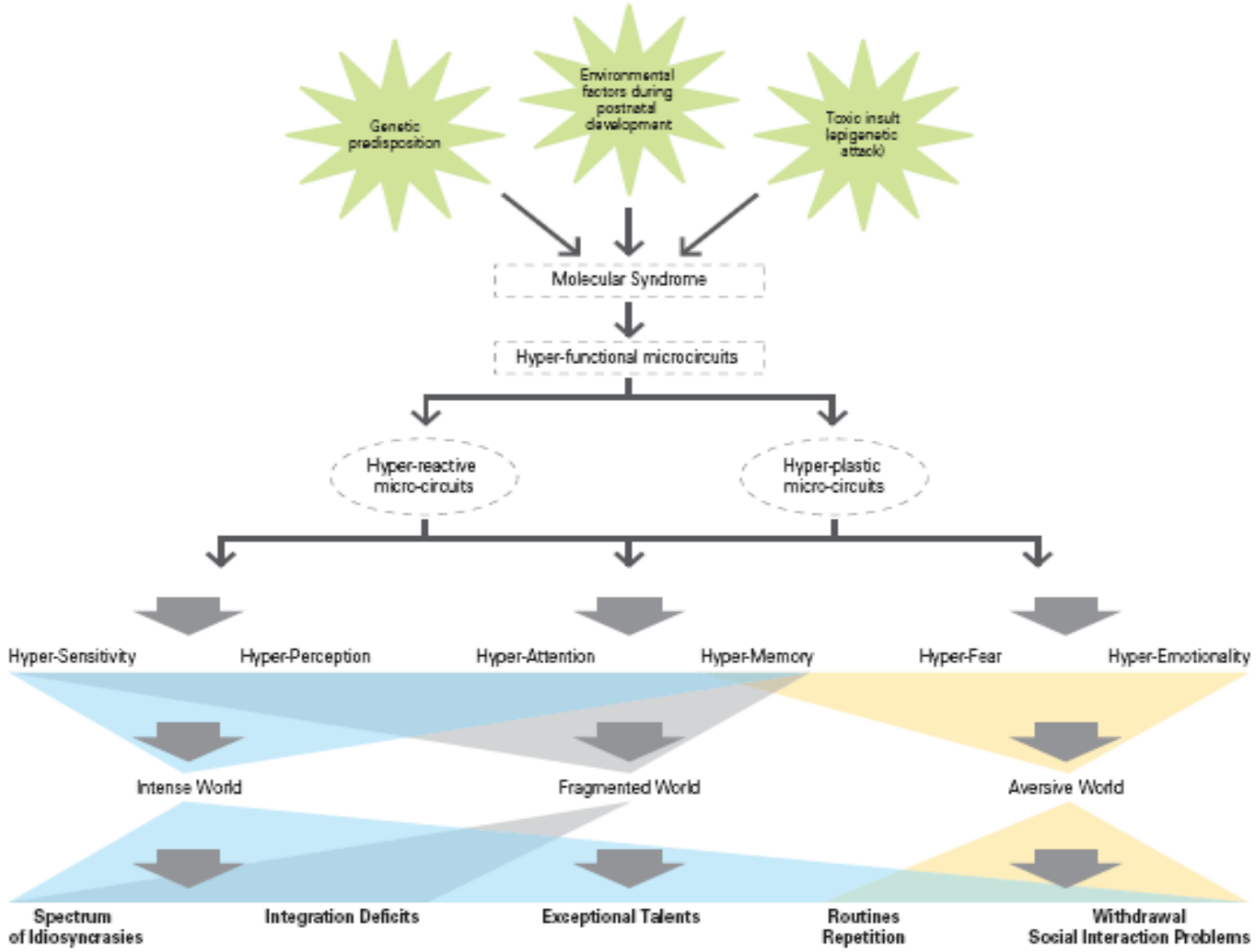


FIGURE 5 | The hyper-functional circuits in autism. As suggested by the *Intense World Theory* three etiological factors (a genetic predisposition; an epigenetics attack in form of a toxic insult; environmental factors during postnatal development) cause autism by activating a molecular syndrome that may be different across different brain regions, but that leads to hyper-functional microcircuits (expressed as hyper-reactivity and hyper-plasticity) in all brain regions. Two regions known to be affected include the neocortex and amygdala and we hypothesize that other regions may be similarly affected. The consequences on cognitive processing include hyper-sensitivity, -perception, -attention, -memory, -fear, and -emotionality. We propose that this leads to an intense, fragmented, and aversive world syndrome for the autistic child, which could account for a spectrum of behavioral abnormalities.

The Intense World theory of AutIsm

- Autonomously acting hyper-functional microcircuits in the neocortex
  - Exaggerated perception to fragments of a sensory world
    - Hyper-focusing on fragments of the sensory world
    - This hyper- attention could become difficult to shift to new stimuli due to the difficulty for bottom-up and top-down mechanisms to coordinate the overly autonomous low-level neocortical columns.
    - The hyper- plasticity component may also further amplify hyper-attention toward the same stimulus and drive over-generalization of attention to all related forms of the stimulus.

The Intense World theory of Autism

- The positive consequences:
  - Exceptional capabilities for elementary and specific tasks while
- The negative consequences:
  - Impairment of holistic processing, a rapid lock to a limited repertoire of behavioral routines
- Local hyper-functionality of amygdala :
  - The intense world that the autistic person faces could also easily become aversive
- The lack of social interaction in autism may therefore is because :
  - A sub-set of cues are overly intense, compulsively attended to, excessively processed and remembered with frightening clarity and intensity.

Intense World theory
A summary

- *A particular form of brain hypertrophy triggered by an epigenetic insult*
  - *May render the brain excessively reactive to the environment*
    - *The excessive reactivity and rapid memory formation of experiences boosted by an amplified emotional component*
      - *may trigger the acceleration of brain maturation until the environment becomes painfully intense.*

Intense World theory
A summary

- *The intensity of lower-order sensory processing becomes so overwhelming that*
  - *The autistic may actively avoid specific features that have become negatively associated and focus on elementary features that have become positively associated.*
    - *Since new information must necessarily be surprising, autistics could rapidly become resistant to rehabilitation.*

Prediction of prognosis According to the Intense World theory

- *The prognosis is proposed to become worse in a sensory enriched and dynamically changing world.*
  - *It is also likely that providing an enriched environment and a directive teaching and aggressive rehabilitation program may in fact accelerate the progression of the disorder.*

Prediction of prognosis According to the Intense World theory

- *The prognosis may be improved by filtering sensory and emotional extremes, preventing surprises, and pharmacologically by suppressing sensory reactivity and memory formation.*
  - *The disorder might even be preventable if intervention begins before the "intense world" reaction is triggered, that is before critical periods of neurodevelopment.*
    - *Reversing consolidated hyper-functional circuits after these critical periods will be more difficult, but due to the potential for learning and memory, an extinction-based rehabilitation program may be effective.*

Behavioral treatment according to the Intense World Theory

- *To focus on filtering the extremes in the intensity of all sensory and emotional exposure as well as relaxation and progressive systematic desensitization to stimuli presentation for the first years of life*
  - *The child should be introduced to new stimuli and tasks gently* and with caution, retracting at any sign of distress.
  - The teacher works carefully to avoid triggering adverse reactions. Introduction to strangers should be controlled, brief, indirect, and as inert as possible.

Pharmacological treatment according to the Intense World Theory

- Focus on:
  - *Reducing brain reactivity in general*
  - *Blocking memory formation*
  - *Reducing stress responses*
  - *Enhancing memory extinction*
- *Blocking NMDA receptors in particular may reduce the hyper-plasticity component of the autistic brains and therefore alleviate some autistic symptoms*
- *Treatment should be applied as early as possible and should last until after the completion of the critical periods of brain development (probably beyond the age of 6).*

Treatment for elderly children and adults According to the Intense World theory

- *Treatment for elderly children and adults with autism would be more difficult to reverse*
  - *Memory attenuation and extinction-based rehabilitation programs as well as reducing anxiety levels and stress responses may at least partially reverse or ameliorate the pathology.*
- *An important consideration in any rehabilitation program is the complication of hyper-emotionality*
  - *Punishments may be greatly amplified for the autistic and imprinted rigorously and indefinitely into the future.*

Conclusions

- This theory is by far not a complete explanation of the cause of autism
  - But it provides a coherent multi-level framework for a complete explanation.
- On a neurobiological level, the *Intense World Theory of autism proposes*
  - *excessive functioning of neural microcircuits,*
    - *with the main symptoms of hyper- reactivity and hyper-plasticity and together, hyper-functionality.*
- *On a perceptual and cognitive level this excessive functioning of local neuronal circuits may lead to*
  - *An intensely perceived world, which may turn aversive and highly stressful if the amygdala and other parts of the limbic system are also affected.*
- Right treatment strategies :
  - Cocooning the autistic infant to protect from surprising situations
  - Dampening brain functioning in early development to prevent driving the brains circuits into an irreversible trajectory

frontiers in
NEUROINFORMATICS

ORIGINAL RESEARCH ARTICLE
published: 24 December 2013
doi: 10.3389/fninf.2013.00037

Information gain in the brain's resting state: A new perspective on autism

José L. Pérez Velázquez*[1,2] *and Roberto F. Galán*[3]*

[1] *Neuroscience and Mental Health Programme, Division of Neurology, Hospital for Sick Children, Toronto, ON, Canada*
[2] *Institute of Medical Science and Department of Paediatrics, Brain and Behaviour Centre, University of Toronto, Toronto, ON, Canada*
[3] *Department of Neurosciences, School of Medicine, Case Western Reserve University, Cleveland, OH, USA*

Edited by:
Daniele Marinazzo, University of Gent, Belgium

Reviewed by:
Jesus M. Cortes, Ikerbasque. Biocruces Health Research Institute, Spain
Filip Van Opstal, Ghent University, Belgium

****Correspondence:***
Roberto F. Galán, Department of Neurosciences, School of Medicine, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106, USA
e-mail: rfgalan@case.edu

Along with the study of brain activity evoked by external stimuli, an increased interest in the research of background, "noisy" brain activity is fast developing in current neuroscience. It is becoming apparent that this "resting-state" activity is a major factor determining other, more particular, responses to stimuli and hence it can be argued that background activity carries important information used by the nervous systems for adaptive behaviors. In this context, we investigated the generation of information in ongoing brain activity recorded with magnetoencephalography (MEG) in children with autism spectrum disorder (ASD) and non-autistic children. Using a stochastic dynamical model of brain dynamics, we were able to resolve not only the deterministic interactions between brain regions, i.e., the brain's functional connectivity, but also the stochastic inputs to the brain in the resting state; an important component of large-scale neural dynamics that no other method can resolve to date. We then computed the Kullback-Leibler (KLD) divergence, also known as information gain or relative entropy, between the stochastic inputs and the brain activity at different locations (outputs) in children with ASD compared to controls. The divergence between the input noise and the brain's ongoing activity extracted from our stochastic model was significantly higher in autistic relative to non-autistic children. This suggests that brains of subjects with autism create more information at rest. We propose that the excessive production of information in the absence of relevant sensory stimuli or attention to external cues underlies the cognitive differences between individuals with and without autism. We conclude that the information gain in the brain's resting state provides quantitative evidence for perhaps the most typical characteristic in autism: withdrawal into one's inner world.

Keywords: brain's resting state, Asperger's syndrome, functional connectivity, stochastic input, relative entropy

Thank for your attention