

### A DEVELOPMENTAL APPROACH TO TICS

### UNDERSTANDING & ADDRESSING THEIR ROOT CAUSE



# Here's how TICS can feel to a child...

WHY CAN'T I STOP?

ITCH I NEED To scratch!!!!

ALL I CAN THINK ABOUT.

I'M JUST A NORMAL KID!

I DON'T WANT TO DISTURB ANYONE.

I DON'T WANT TO BE EMBARRASSED ANY MORE.

.

IT KINDA

WIERDS ME

0UT...

Source: From the HBO documentary"I Have Tourette's But Tourette's Doesn't Have Me" (2005)



### PATTERNS CLASSIFIED AS TIC "DISORDERS"

#### Classification based on observed symptoms

- Number of specific tics
- Type of tics
- Age of onset
- Frequency
- Duration of symptoms

#### **Tourette Syndrome (TS)**

- 2+ motor tics *and* 1+ vocal tic
- 1+ years duration, nearly every day
- Onset before age 18
- Tics not due to medication / condition

#### **Persistent (Chronic) Tic Disorder**

- 1+ motor or vocal tic(s), but *not* both.
- 1+ years, many times nearly every day
- Onset before age 18
- Tics not due to medication / condition

#### **Provisional Tic Disorder**

- 1+ motor or vocal tic(s)
- Under 12 months in a row
- Onset before age 18
- Tics not due to medication / condition
- No TS / persistent tic disorder diagnosis

#### Source: cdc.gov



### WHAT ARE TICS?

• Tics: sudden twitches, movements, or sounds that people do repeatedly

Motor ticsSimple ticsVerbal ticsComplex tics

- Current scientific thinking about the source of tics
  - Genetic?

"Tourette syndrome genetics research has been frustrating. Despite an apparent high heritability, association studies are largely barren."

- Dopamine / neurochemistry?
  *"There is little evidence of abnormalities of striatal dopaminergic innervation in Tourette syndrome."*
- Functional connectivity?

Increasing evidence of **circuitry problems** of the brain systems associated with social decision making (SDM), within the social behavior network (SBN)

Source: cdc.gov, Roger L Albin, Tourette syndrome: a disorder of the social decision-making network, Brain, Volume 141, Issue 2, February 2018, Pages 332–347.



# CIRCUITRY PROBLEMS

"The emergence of involuntary movements, vocalizations and subsequent natural history of Tourette syndrome follows a predictable pattern in the first 2 to 3 decades of life, suggesting that Tourette syndrome results from altered brain development trajectories."

Source: L Albin, Tourette syndrome: a disorder of the social decision-making network, Brain, Volume 141, Issue 2, February 2018, Pages 332–347.



### ADDITIONAL "TRUISMS" REGARDING TICS

- Age of onset is typically middle childhood (6-10 yo), more frequent in boys than girls
- Symptoms are intermittent (i.e. appear, disappear, reappear)
- Tics can seriously impede daily function, interfering with school, work, or social life, and can
  - Generate feelings of embarrassment and stress
  - Tire and distract during the activity of suppression
  - Cause pain or injury
- Co-morbid w/ other NEURODEVELOPMENTAL issues (ADHD, anxiety, OCD, ASD, LDs, SPD, etc.)
- Medication / behavioral treatments have limited effectiveness, but there's no cure
- Tics most often decrease during adolescence & early adulthood, often disappearing entirely
  - Compensatory neuroplastic changes in the brain allow the individual's brain to "catch up"

Source: cdc.gov, Compensatory neural reorganization in Tourette syndrome, Stephen R Jackson et al. Curr Biol. 2011.



## WAIT...WHAT?

:01





### Neuroplastic changes

### in brain structure & connectivity

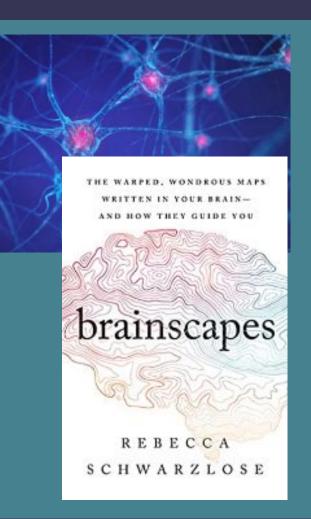
### control tics

over time, helping the brain onto a more typical developmental trajectory.

# NEUROPLASTIC CHANGE? WHAT'S THAT?

#### The Human Brain: An Organ of "Surreal Complexity"

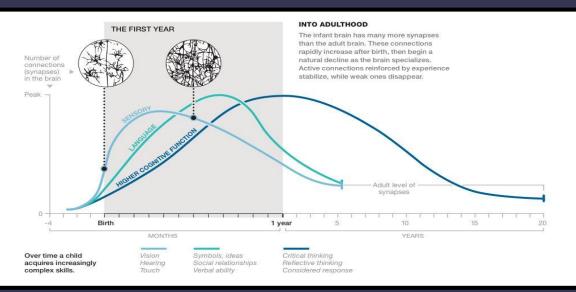
- The most complicated organ known in nature
  - ~ 100 billion neurons (brain cells) form ~ 100 trillion connections
  - "Neurons that fire together, wire together"
  - Functional connections in the brain are the basis of learning
- Typical wiring ("functional connectivity") = the "Human Connectome"
  - Enables typical self-regulation, skill mastery, etc.
- Disorders involve **predictable** differences in functional connectivity
  - Wiring differences are **detectable** ahead of symptoms
- The brain can change. It remains neuroplastic throughout our lives



## BUILDING THE HUMAN CONNECTOME







- Brain wiring depends heavily on environmental input
  - Being born with the right "equipment" is not enough
  - Experiences & stimulation drive development
- "Lightning pace of development" in the first few years
  - Different stimuli / tasks establish different networks
  - Repeated activation strengthens / refines circuits
  - Dysfunction is observable when brain wiring is not typical
  - Appropriate intervention exists and is highly effective
    - Strengthens existing connections
    - Builds connections not previously formed
    - Improves self-regulation, learning, skill mastery, etc.

Source: Bhattacharjee, Yudhijit, "The First Year", National Geographic, January 2015.



### NEUROPLASTICITY'S ROLE IN OVERCOMING TICS

- Increasingly, TS research is focused on the functional connectivity within a system of brain regions
- These regions "learn" to work together in the way we consider "typical" over time
- Suppression of tics is a part of typical human development, much like social and emotional learning, academic learning, physical coordination, etc.

"Increased control over motor outputs, including suppression of tics, may develop during adolescence in TS and be accompanied by compensatory, neuromodulatory, alterations in brain structure & function."

	tory Neural Reorg	Report ganization
Stephen R. Jackson, 1.2.	* Amy Parkinson, <sup>2</sup> Jeyoung Jung, <sup>1</sup>	TS [1-6]. Thus, it is suggested that children and adolescents
Suzanne E. Ryan, <sup>2,3</sup> Paul S. Morgan, <sup>4</sup> Chris Hollis, <sup>3</sup> and Georgina M. Jackson <sup>3,*</sup> <sup>1</sup> WCU Department of		with TS gain control over their tics through the development of compensatory self-regulation mechanisms, most likely
Korea University, Seo <sup>2</sup> School of Psycholog		
Nottingham NG7 2RD <sup>3</sup> Division of Psychiatr		PLOS COMPUTATIONAL BIOLOGY
A Floor, South Block, Nottingham NG7 2UH <sup>4</sup> Department of Acad Nottingham, Nottingh	RESEARCH ARTICLE	BIOLOGY
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Children with neuro developmental trajec satory neuroplastic c that help them gain used behavioral and l	Tourette synd	Irome
	Daniele Caligiore <sup>1</sup> *, Francesco Mannella <sup>1</sup> , Michael A. Arbib <sup>2</sup> , Gianluca Baldassarre <sup>1</sup>	
this conjecture in c Using a behavioral ta nual conflict, we si enhanced control of (diffusion-weighted i	National Research Council (CNF	mbodied Neuroscience, Institute of Cognitive Sciences and Technologies 3-ISTC-LOCEN), Roma, Italy, <b>2</b> Neuroscience Program, USC Brain Projec University of Southern California, Los Angeles, California, United States o
in Cognitive Sc	iences	CelPress

#### Opinion

Inhibition, Disinhibition, and the Control of Action in Tourette Syndrome

Georgina M. Jackson,<sup>1,\*</sup> Amelia Draper,<sup>2</sup> Katherine Dyke,<sup>2</sup> Sophia E. Pépés,<sup>2</sup> and Stephen R. Jackson<sup>2,\*</sup>

Tourette syndrome (TS) is a neurological disorder characterized by vocal and motor tics. TS is associated with impairments in behavioral inhibition, dysfunctional signaling of the inhibitory neurotransmitter GABA, and alterations in the balance of excitatory and inhibitory influences within brain networks implicated in motor learning and the selection of actions. We review evidence that

Terricus Tourette syndrome (TS) has been linked to impairment of inhibitory function. Recent evidence provides support for reduced physiological inhibition as a factor in the occurrence of tics. hui iated with y supports

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proposes



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**bIAMY** 

Mesolimbio

Reward System

### A "SYSTEM PERSPECTIVE"

- Neuro-anatomical system
  - Basal ganglia work together with the cortex and cerebellum
  - Selection and maintenance of appropriate responses
    - Generate behaviors of various complexity
    - Inhibit inappropriate responses
- Systemic differences in Tourette's Syndrome
  - Related brain structures are immature
  - Atypical interactions/functional connectivity between regions
- Same "dysfunction" is also implicated in OCD and ADHD

Cortex Basal ganglia Thalamus Cerebellum



"ADHD is common in TS, as are anxiety disorders [and] obsessive compulsive behaviours, often arising to the level of OCD. It is plausible to view simple tics and complex obsessions as opposite poles of a spectrum with compulsive behaviours occupying the middle of the spectrum"

Source: Roger L Albin, Tourette syndrome: a disorder of the social decision-making network, Brain, Volume 141, Issue 2, February 2018, Pages 332–347.



### CATEGORIES OF COMPLEX LEARNING / SKILL MASTERY

**Executive Function** 

Academics - Social Skills

**Behavior - Anxiety** 

Focus - Attention - Cognition

THE FOUNDATION OF LEARNING Processing "the ability to learn".

**Fine Motor Function** 

#### **Gross Motor Functions**

Making sense of / tolerating complex environments, feeling our bodies

Purposeful regulation / voluntary control, visual integration, vestibular security

Sensory Processing (see, hear, smell, feel)

**`Primitive** Reflexes

Comprehension, reasoning, making inferences, reading social cues

Precision, grip, manual dexterity, eye tracking, writing, buttons/zippers

Walking, running, coordination, stamina, strength, posture, engagement

### THE PROMISE OF PLASTICITY-BASED INTERVENTIONS



#### **Dr. Michael Merzenich,** Neuroscientist & Author:

"Brain plasticity-based therapeutics can be expected to drive fundamental re-normalizing corrections for distorted brain systems."

- Neurodevelopmental disorders: "failure modes of the self-organizing brain"
- We have clear insight into brain-changing processes
  In the degrading, aging, distorting direction
  - In the strengthening, rejuvenating, corrective direction
- Brain "remodeling" can be induced
  - On a large scale
  - At any age

#### frontiers in HUMAN NEUROSCIENCE



#### Brain plasticity-based therapeutics

#### Michael M. Merzenich<sup>1</sup>\*, Thomas M. Van Vleet<sup>1,2</sup> and Mor Nahum<sup>1,3</sup>

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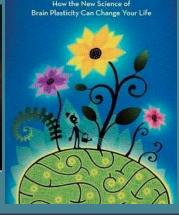
Gitendra Uswatte, University of ph Alabama at Birmingham, USA ph **\*Correspondence:** that Michael M. Marsenich, Brain pal Plasticity Institute at Posit Science Corporation, 77 Geary Street, Key Rm. 303, San Francisco, CA 94108,

The primary objective of this review article is to summarize how the neuroscience of brain plasticity, exploiting new findings in fundamental, integrative and cognitive neuroscience, is changing the therapeutic landscape for professional communities addressing brain-based disorders and disease. After considering the neurological bases of training-driven neuroplasticity, we shall describe how this neuroscience-guided perspective distinguishes this new approach from (a) the more-behavioral, traditional clinical strategies of professional therapy practitioners, and (b) an even more widely applied pharmaceutical treatment model for neurological and psychiatric treatment domains. With that background, we shall argue that neuroplasticity-based treatments will be an important part of future best-treatment practices in neurological and psychiatric medicine.

Keywords: brain plasticity, neuroplasticity, computer

DR MICHAEL MERZENICH PHD

REPUNDATION CERVER TIVE NEUROSCIENCE





### LEVERAGING BRAIN PLASTICITY

■ Intensive, integrated, targeted, strengthening exercise

- Sensory engagement
- Physical exercise
- Academic / cognitive activities
- Progressively challenging, purposeful
- Must reflect complexity of real world to change brain
- Improves speed & efficiency of neural pathways
  - Key networks in the brain fire, then wire, together
  - Drives synchronization of skills
- Brain connections become more typical
- Leads to more typical function
  - Self-regulation
  - Information processing
  - Learning





# HOW DO WE KNOW THE APPROACH WORKS?

#### Harvard/McLean Findings

- "Profound effects" in terms of
  - Symptom improvement
  - Measured attention
  - Functional brain connections
- Multiple assessments
  - Pre-study (Test 1)
  - Immediately after 16 weeks of participation (Test 2)
  - ½ year post-study (Test 3)
- Persistence of benefits due to true neuroplastic change

#### Replicable Results / Parent-Reported Success Stories

"LIFE CHANGING in the most positive way" "It's just absolutely amazing what he's accomplished." "He's been on the school news here 6 or 7 times already doing weather reports, news reports, things like that." "1.5 years later...99% better...occasionally make a snorting noise...interacts with friends...a normal social life."

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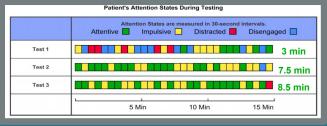


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White Paper: Profound Effects of Brain Balance Exercises and Interactive Metronome and on a Subset of Children with Attention Deficit Hyperactivity Disorder





# IN SUMMARY:

### By promoting beneficial neuroplastic change, we can help people **control tics sooner**.



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# ANY QUESTIONS?

#### RESOURCES

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