



Neurological Diseases:
**Autism spectrum
disorders**

8.1.2020

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Recap and Survey

Join at www.kahoot.it
(phone, tablet, or
computer are OK)

With Game PIN

104379

We will start the game
when everyone has joined

Is there a neurological
disease we haven't
covered so far that you'd
like to learn about?

Send it in the Chat!

We will run a poll after the
Kahoot to decide the
topic for our last class.

Course outline

7/11 Intro to neuroscience
Epilepsy & brain lesions

7/18 Alzheimer's disease

7/25 Parkinson's and Huntington's
disease

8/1 Autism spectrum disorders

8/8 Anxiety & PTSD

8/15 Student's choice!



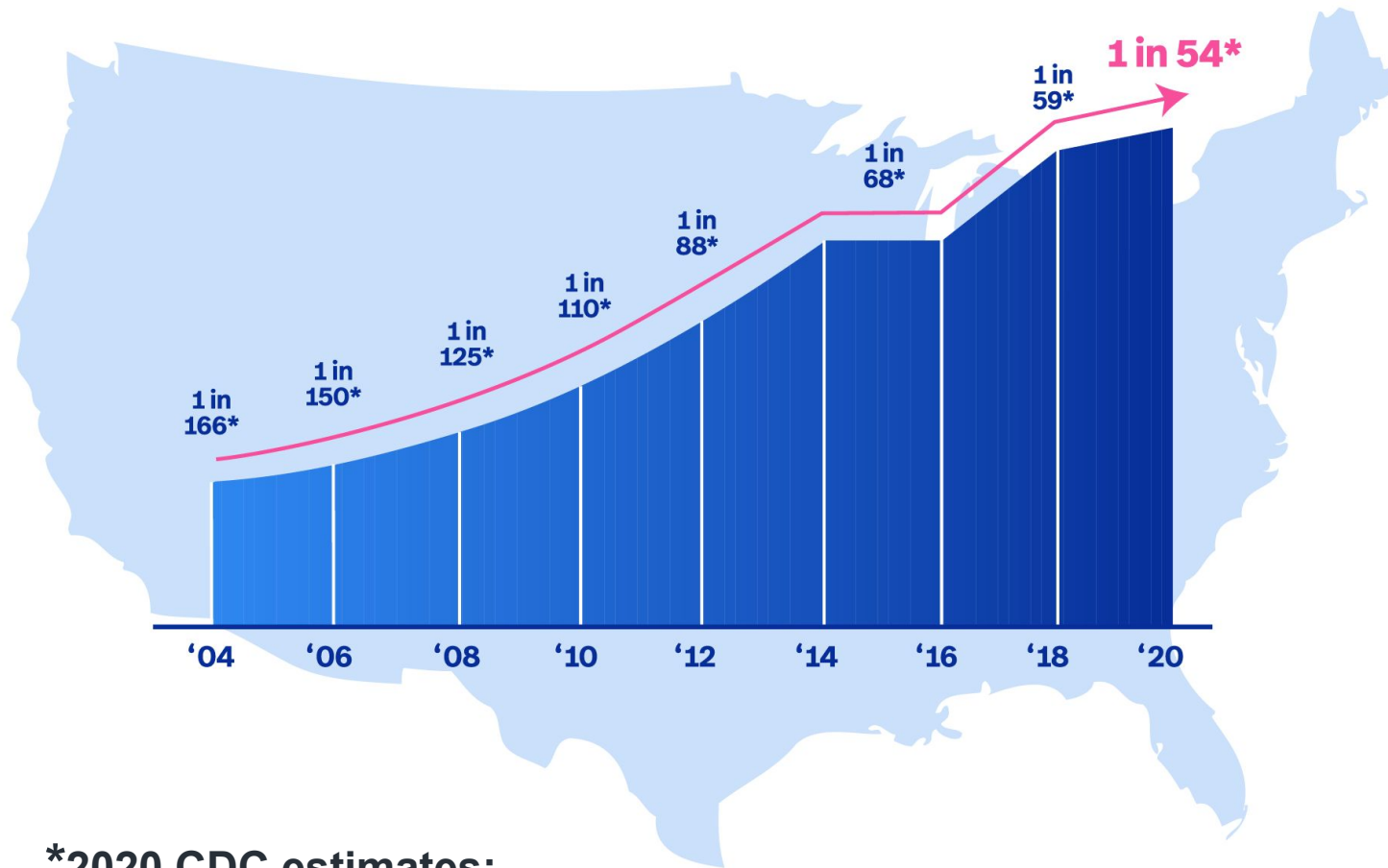
People with autism are people

#ActuallyAutistic



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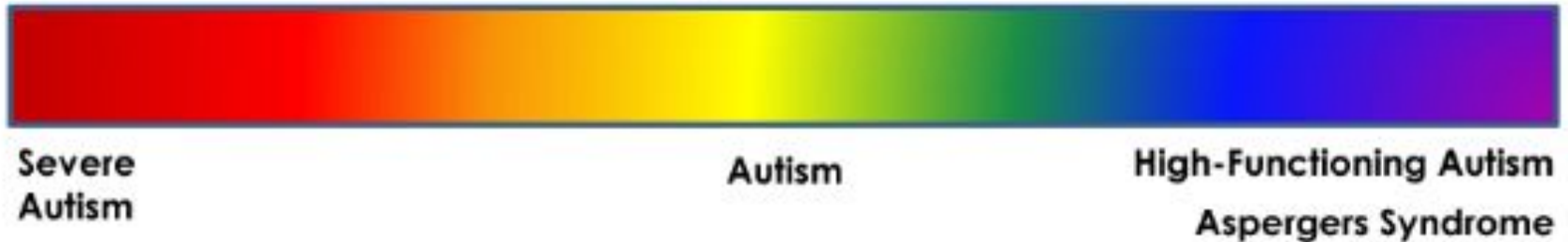
Estimated Autism Prevalence 2020



*2020 CDC estimates:

- 1 in 34 boys
- 1 in 144 girls
- All ethnic and socioeconomic groups

The autism spectrum



General Symptoms/presentation

- Difficulty with communication and interaction with other people
- Restricted interests and repetitive behaviors
- Symptoms that hurt the person's ability to function properly in school, work, and other areas of life

-
- It's a spectrum: wide variation between people!
 - Diagnosis occurs in children, as young as 2 yrs old

The Three Functional Levels of ASD

ASD Level 1 Requiring Support



difficulty initiating social interactions

organization and planning problems can hamper independence

ASD Level 2 Requiring Substantial Support



social interactions limited to narrow special interests

frequent restricted/repetitive behaviors

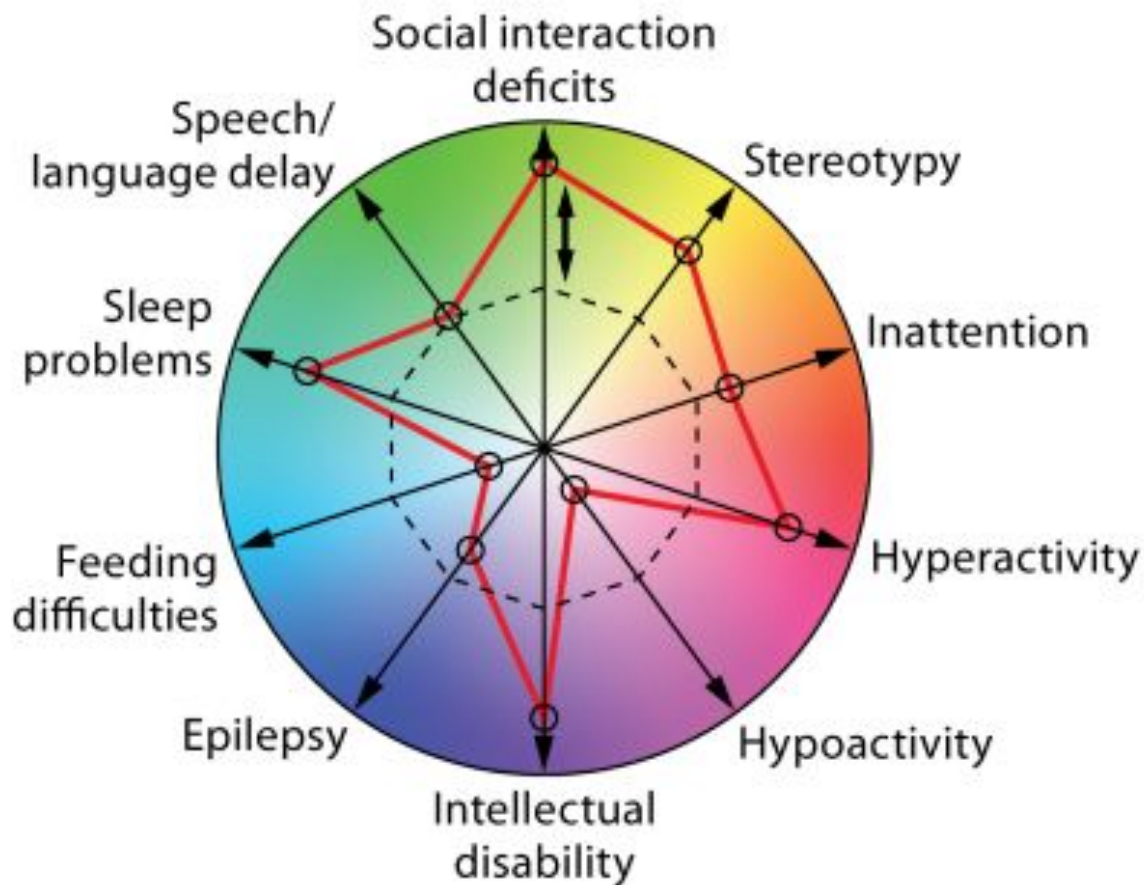
ASD Level 3 Requiring Very Substantial Support



severe deficits in verbal and nonverbal social communication skills

great distress/difficulty changing actions or focus

The autism spectrum: Not always a line



*Example of one patient's presentation

Comorbidities

Comorbid Disorder	Rate of patients (%)
Attention deficit/Hyperactivity disorder	66
Bipolar disorder	18.4
Psychosis	15.8
Depression	5.3
Tics and Tourette's syndrome	5.3
Generalized anxiety disorder	5.3
Oppositional defiant disorder	5.3
Eating disorder	2.6
Obsessive/Compulsive disorder	2.6
Learning disorder	2.6
Epilepsy	30%
Intellectual disability	31%

The autism spectrum

Repetitive behaviors:

- Rules and routine are important
- Change is stressful

Specific interests:

- Often pick a particular topic of interest & learn a lot about it



The autism spectrum

Sensory issues:

- Sensitive to loud noises/bright sounds
- Inability to “tune out” the noise



The autism spectrum

Social issues:

- Difficulty identifying emotions
- Difficulty understanding subtle signals like body language & tone
- Social interactions are hard!



What causes ASD?

Potential causes:

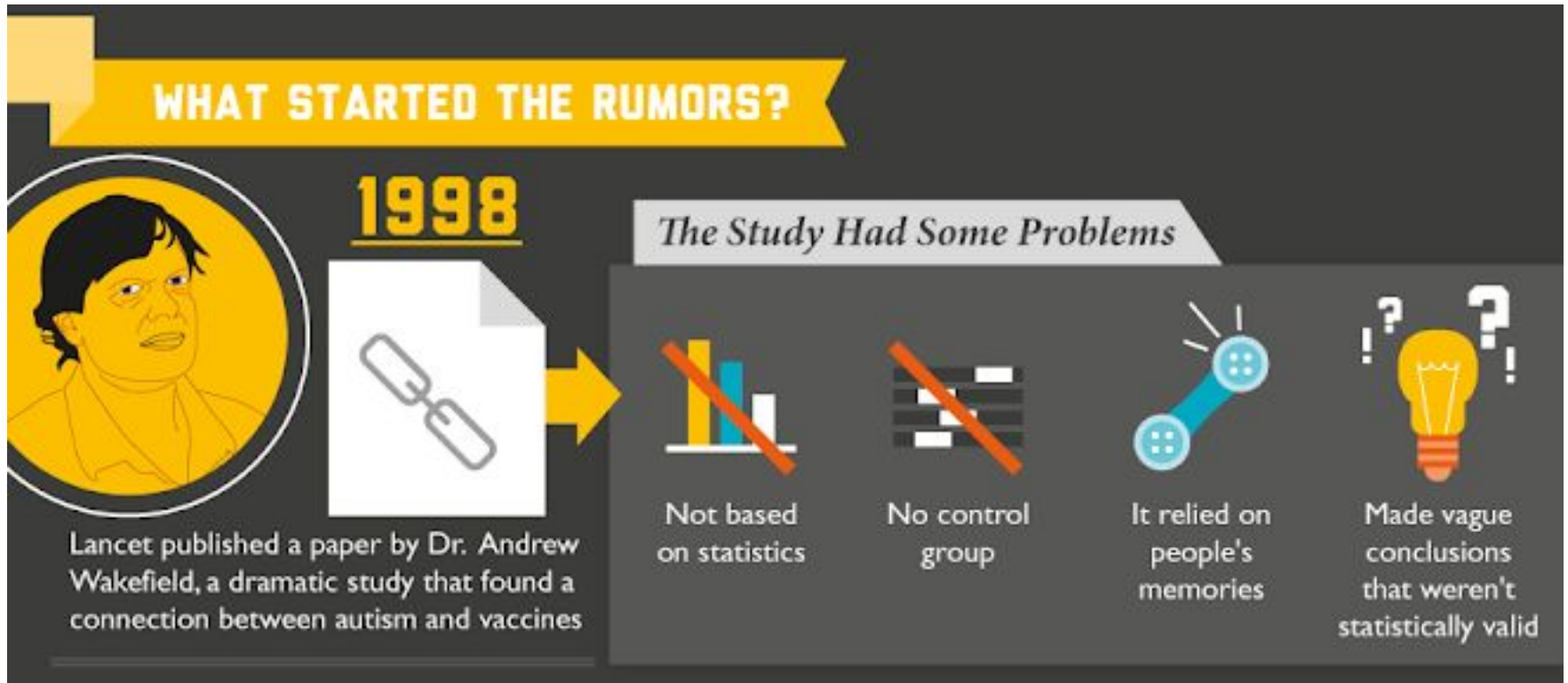
- Genetics
- Low birth weight
- Age of parents
- Environmental factors
- ???

Factors that DO NOT cause ASD:

- Vaccines
- Being around someone who has ASD
- Bad parenting
- Bad diet



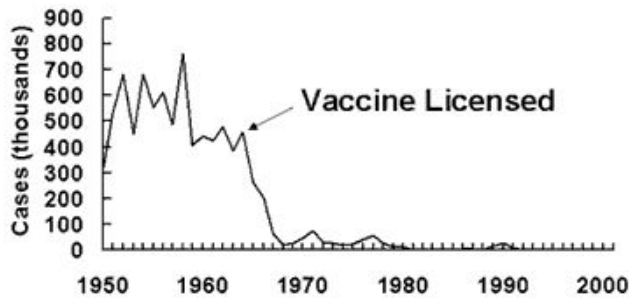
Tangent: Vaccines and autism



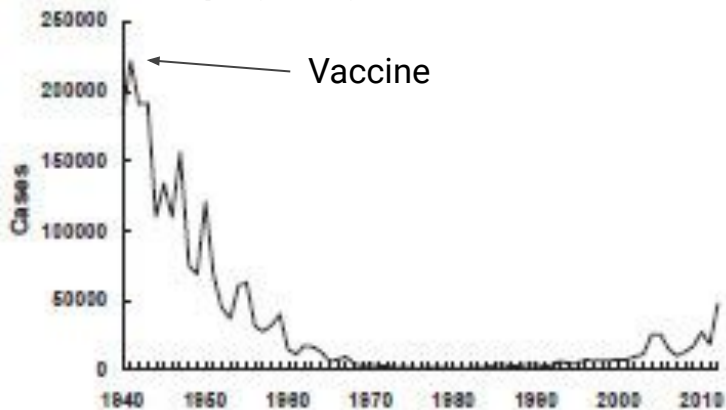
Many subsequent studies of up to 14 MILLION children failed to find any connection between vaccines and autism

Tangent: Toll of the anti-vaccine movement

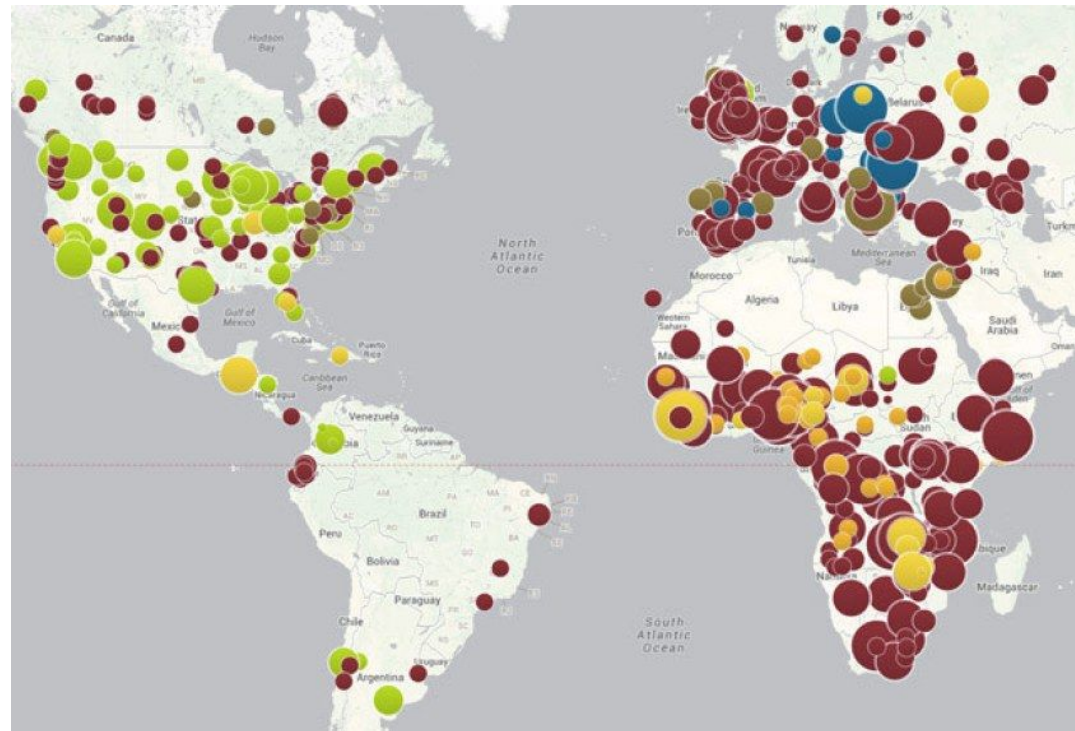
Measles—United States, 1950-2001



Whooping Cough-US, 1940-2010

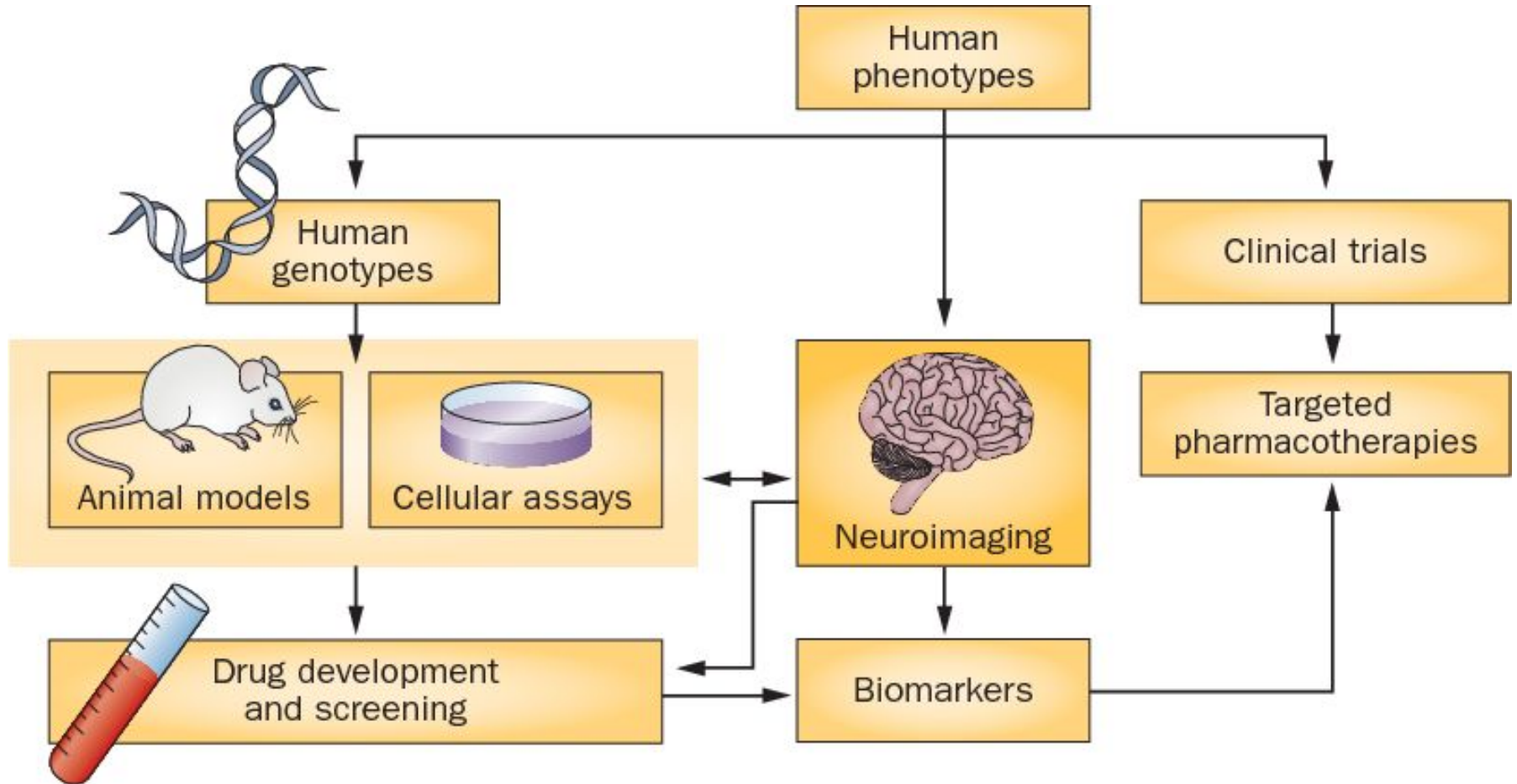


Vaccine-preventable disease outbreaks, 2008-2014

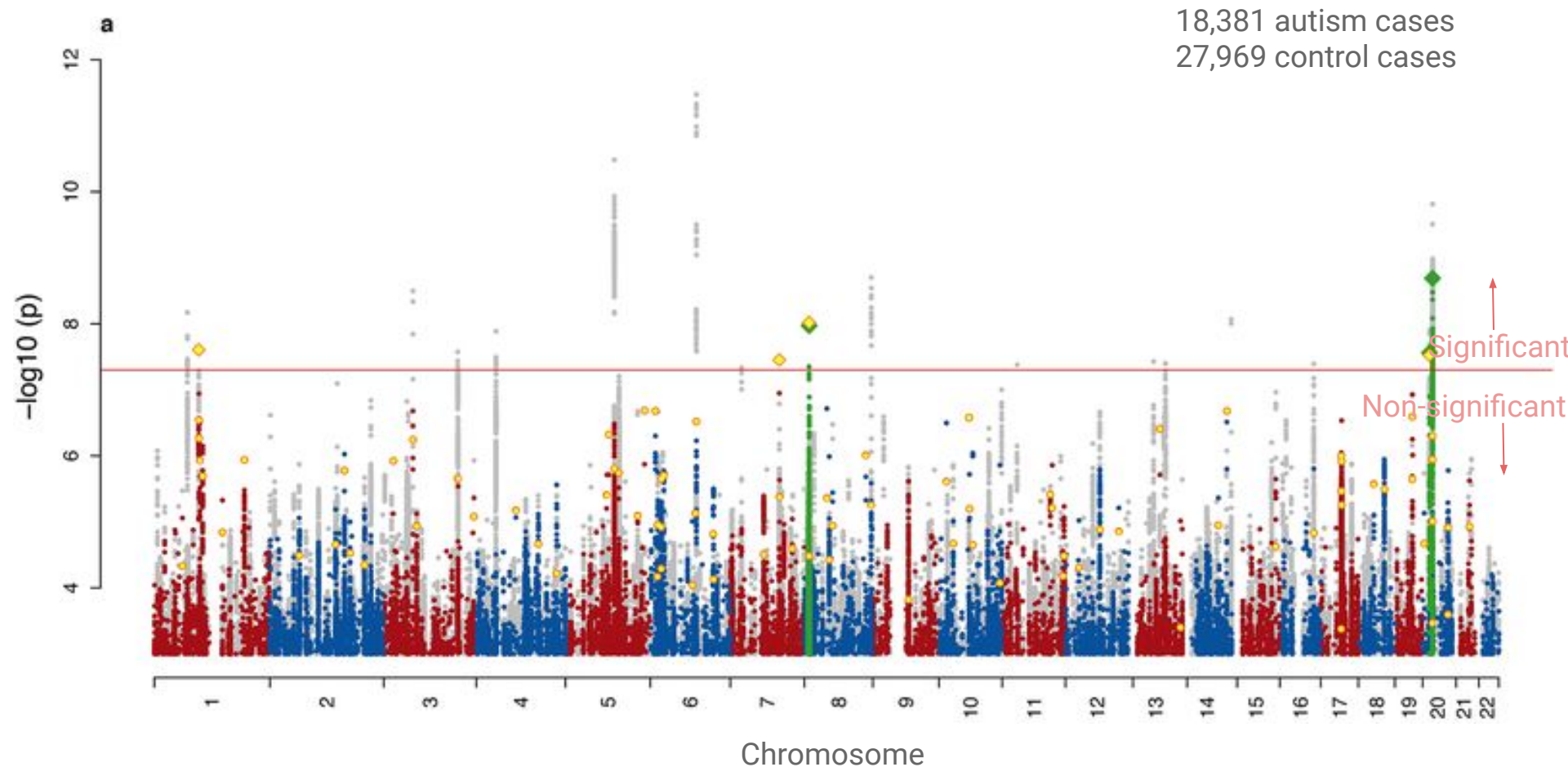


Measles outbreaks
Whooping cough outbreaks
Graphic from LA Times, 2014

How do we study ASD?



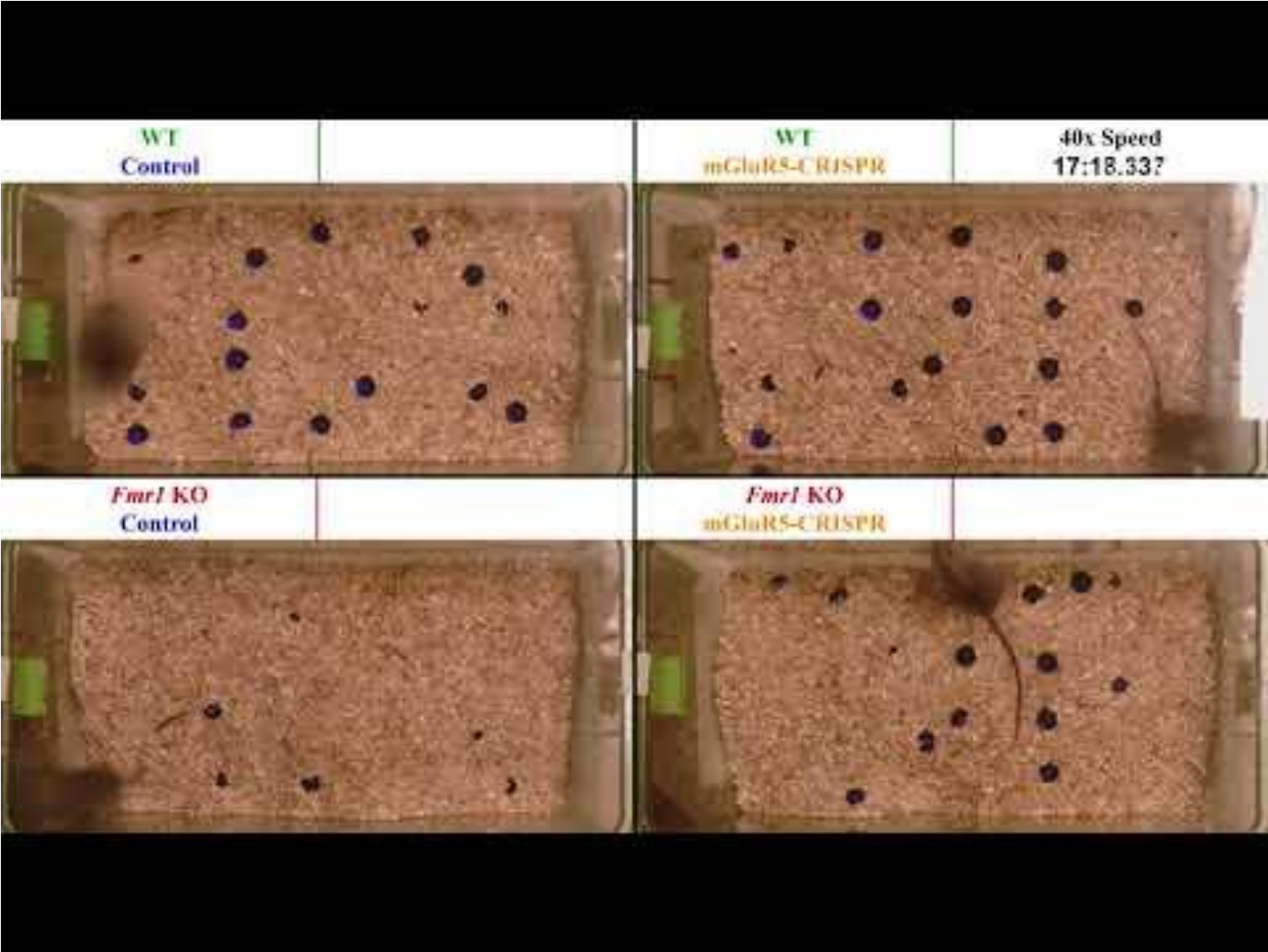
Genetics of autism: Genome Wide Association Study (GWAS)



Mouse models of ASD

Gene	SFARI classification	Mouse model	Phenotype
CNTNAP2	syndromic	<i>Cntnap2</i> ^{-/-} mice	ASD core behavioural symptoms, hyperactivity and seizures, loss of GABAergic neurons in the cortex, striatum and hippocampus
FMR1	syndromic	<i>Fmr1</i> KO mice	Attentional dysfunction Social anxiety and impaired social cognition Ultrasound vocalization deficits Seizures Reduced expression of GABA _A receptor subunits Altered GABAergic transmission Loss of PV cortical interneurons
MECP2	syndromic	<i>Viaat-Mecp2</i> conditional mutant mice	ASD-like repetitive and stereotyped behaviours, EEG abnormalities and seizures, reduced GAD65/67 mRNA in the cerebral cortex, decreased cortical miniature inhibitory post-synaptic currents
NF1	syndromic	<i>Nf1</i> ^{+/-} mice Mice lacking <i>Nf1</i> in interneurons	Deficits in early-LTP and spatial learning Over-activation of Ras signaling in inhibitory interneurons during learning, abnormal enhancement of GABA release
PTEN	syndromic	Mice lacking <i>Pten</i> in the cerebral cortex and hippocampus	Altered social behaviour and inappropriate responses to sensory stimuli
SHANK3	syndromic	<i>Shank3B</i> mutant mice <i>Shank3A</i> mutant mice <i>Shank3(e4-9)</i> mutant mice	ASD-like features (repetitive grooming, reduced social behaviours) Milder phenotype than <i>Shank3B</i> mice (normal social behaviours and reduced recognition of social novelties) Abnormal social and repetitive behaviours, impaired learning and memory

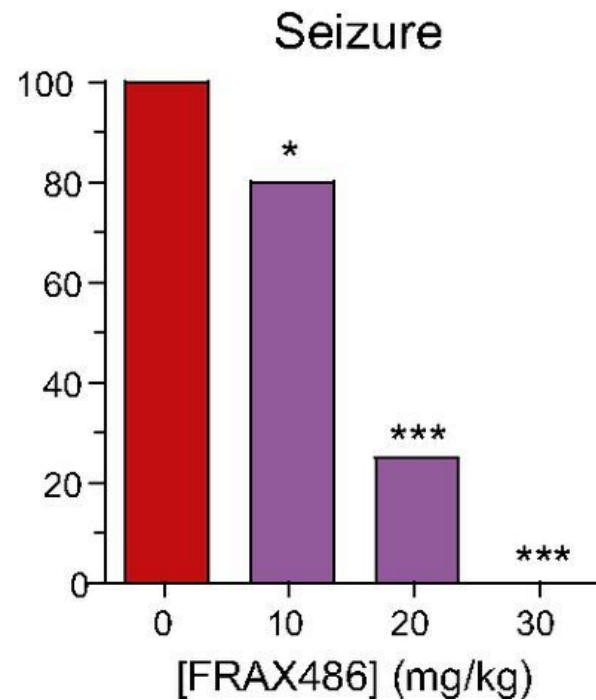
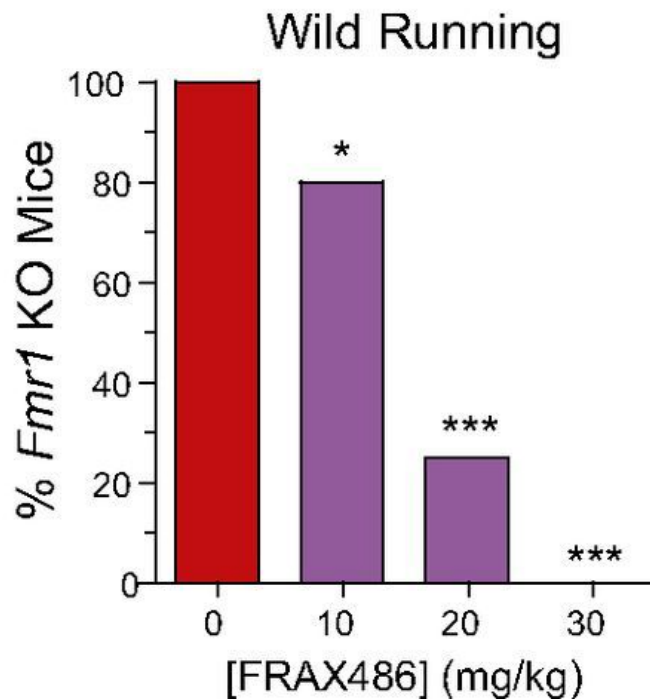
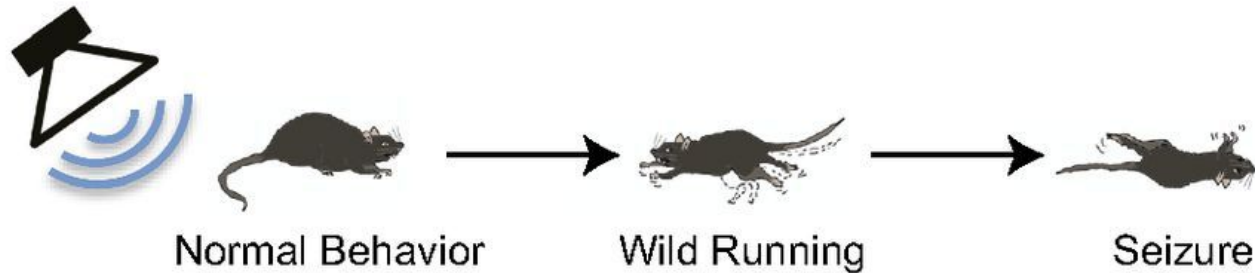
Repetitive behavior assay



Social deficit assay



Seizure susceptibility assay



ASD is complex!

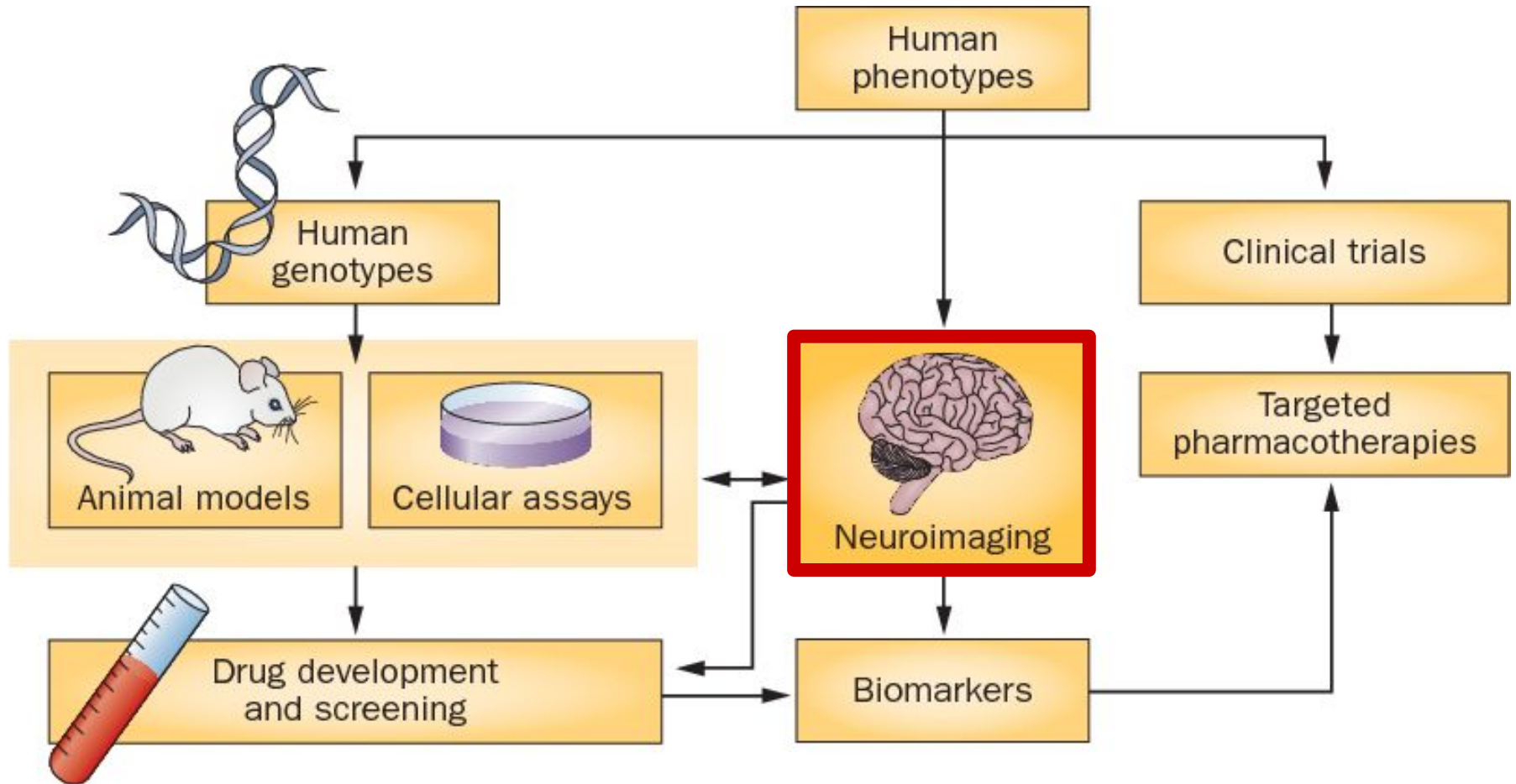
ASD-linked genes have direct effects on:

- Transcription
- Translation
- Synapse scaffolding
- Cell adhesion
- Receptors

...which lead to indirect effects on:

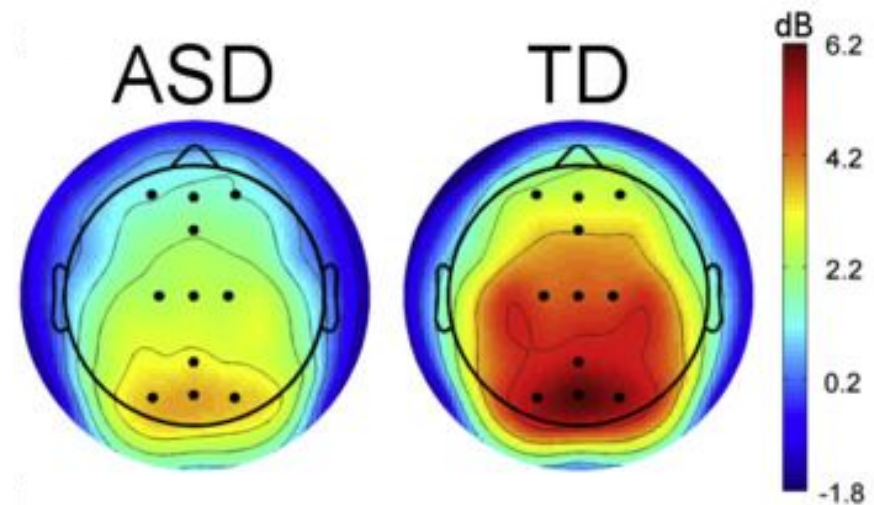
- Synapse function
- Excitatory/inhibitory balance
- Circuitry in different brain regions

How do we study ASD?



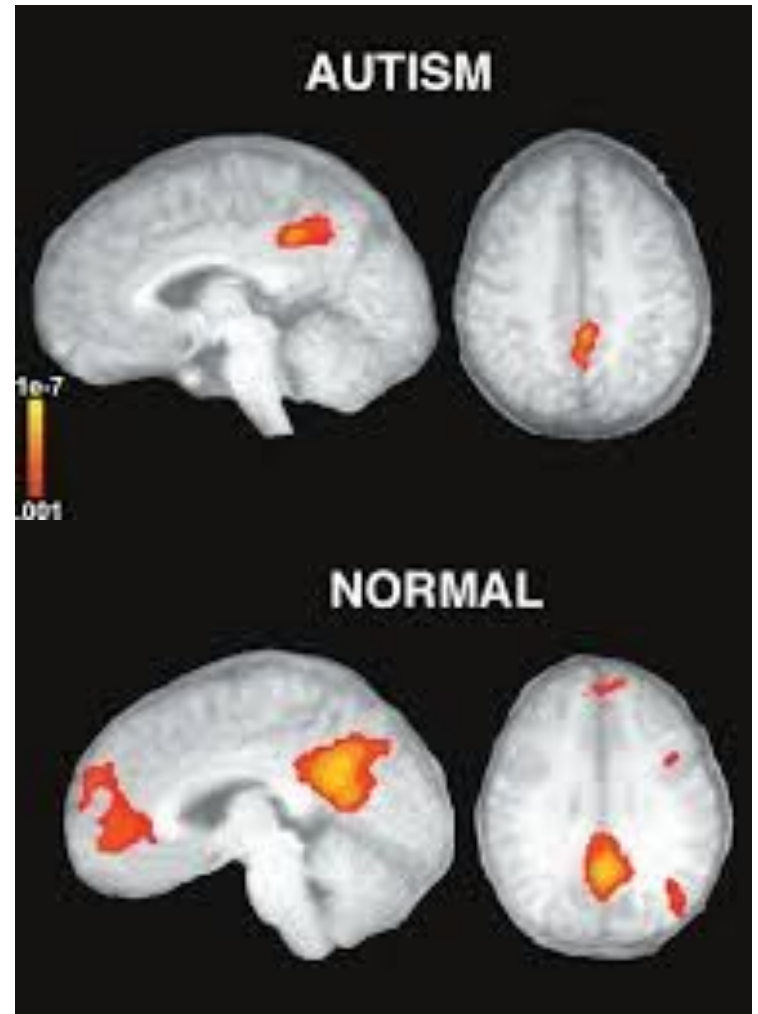
Brain imaging to study ASD

Electroencephalography (EEG) used to measure neural oscillations



Deficits in social brain areas

Functional Magnetic Resonance Imaging (fMRI) measures activity in different brain regions



Questions ?

