“天使们”不想孤独

—孤独症研究及治疗方案

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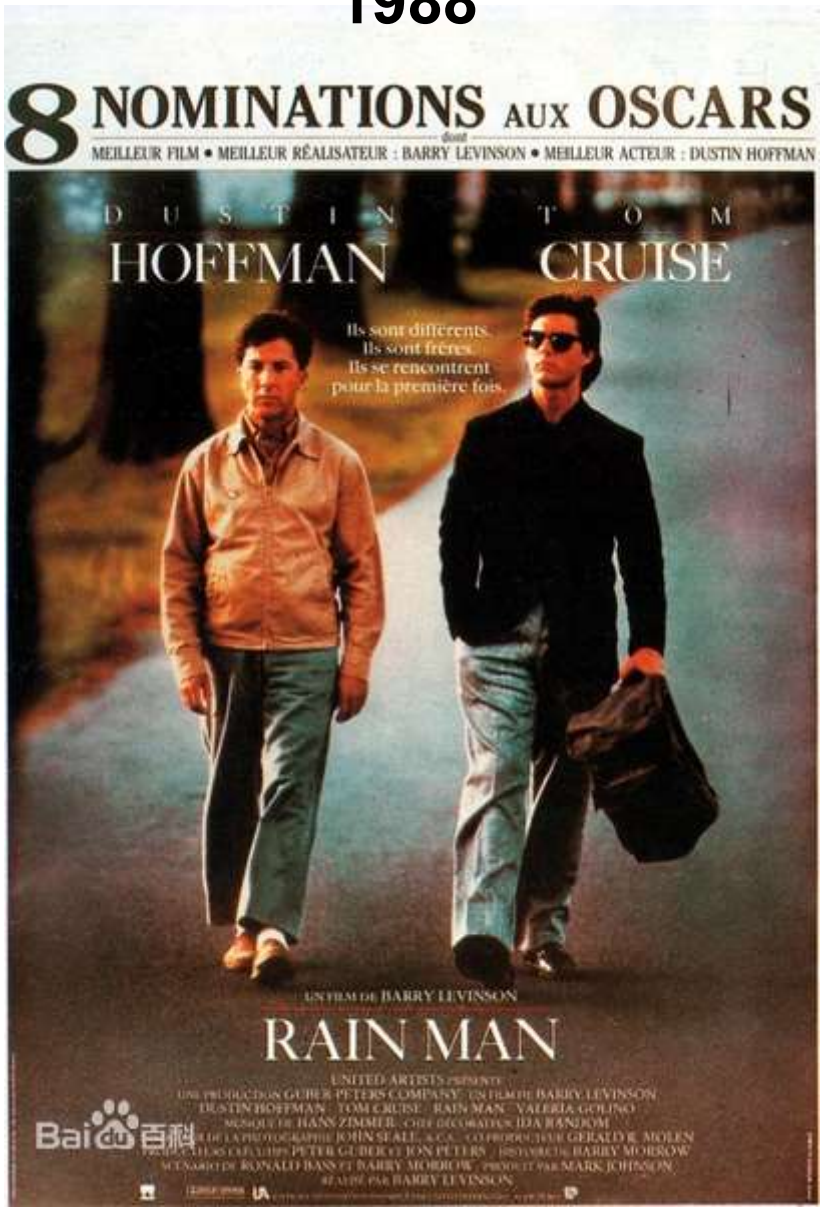
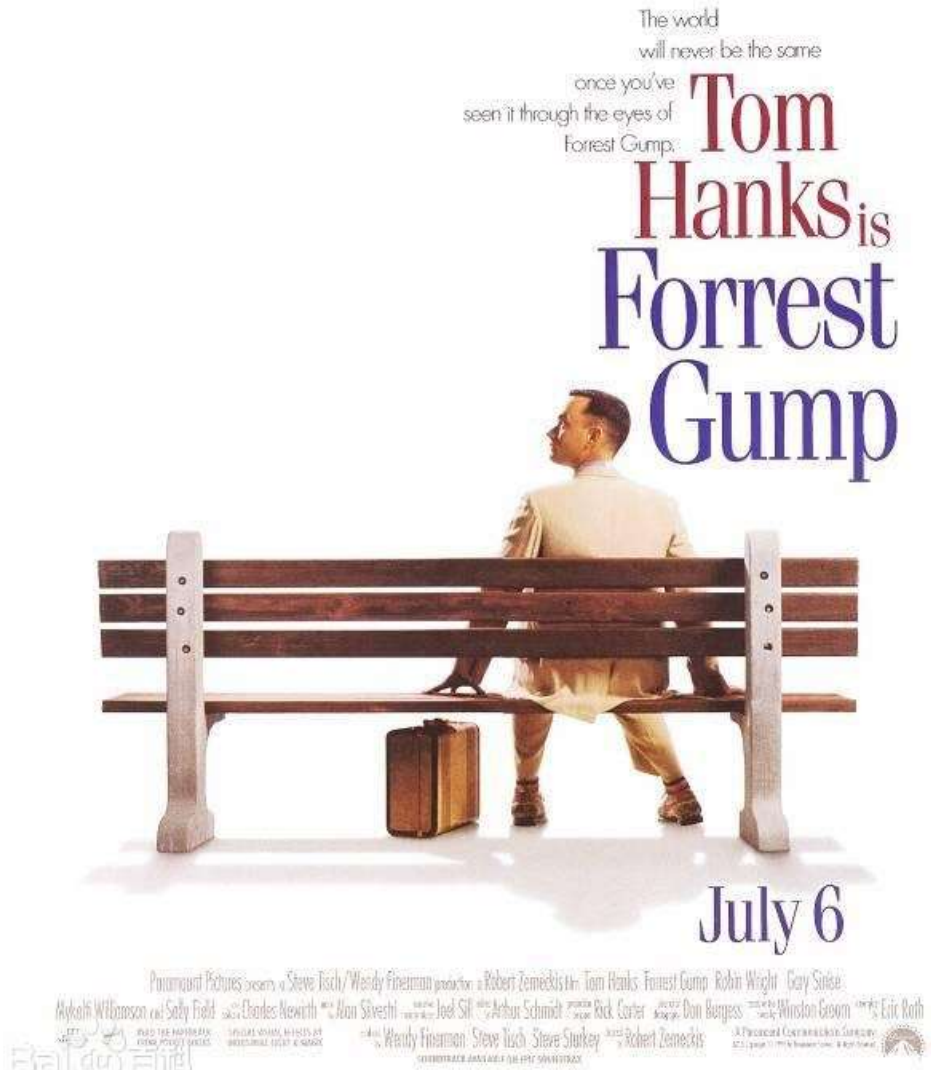
2020/05/11

雨人
1988



阿甘正传
1994



什么是孤独症？

孤独症 (ASD)，又称自闭症，是一种严重的先天中枢神经发育障碍性疾病。

根据美国疾病控制与预防中心 (US CDC) 2014年发布的数据，8岁儿童人群的发病率为1.68%。该病男女发病率差异显著，男孩发病大致高于女孩4倍。

典型自闭症核心症状就是所谓的“三联症”，主要体现为在语言交流障碍、社会交往困难和重复刻板行为三个方面同时都有缺损，并伴有睡眠和胃肠功能异常。

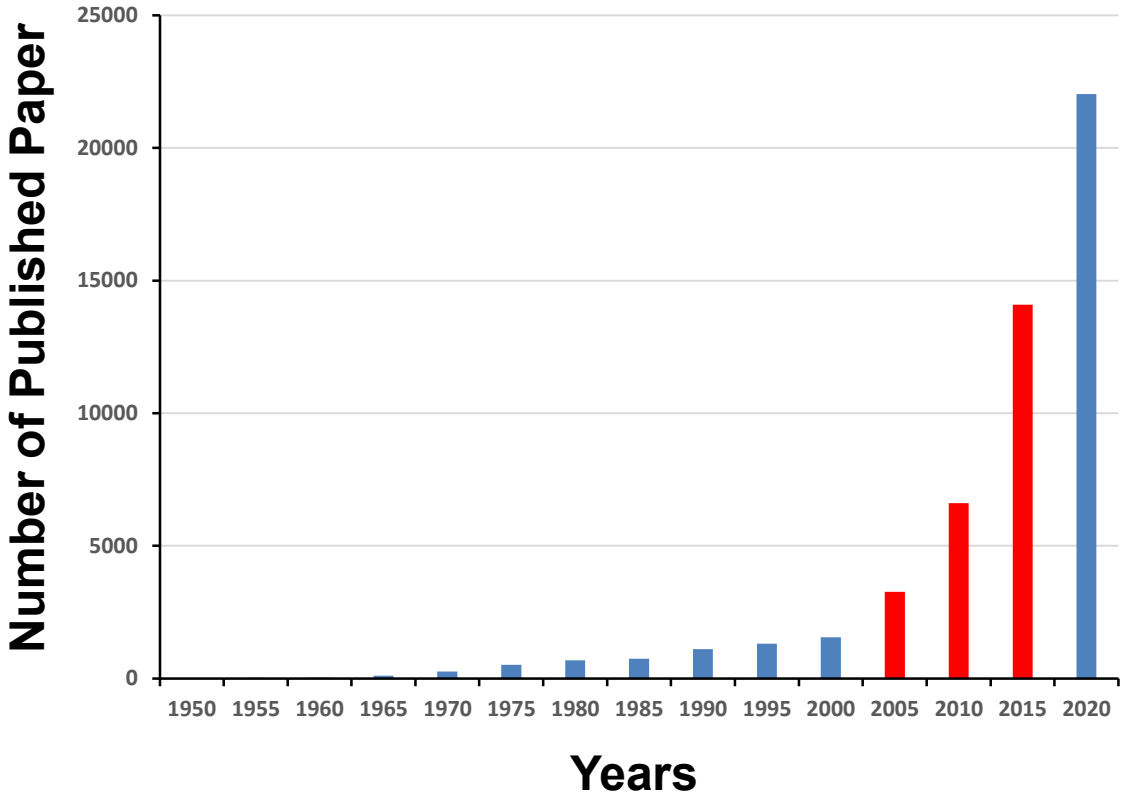
Leo Kanner与孤独症？

Leo Kanner
(June 13, 1894 – April 3, 1981)
Father of child psychiatry

1. Leo Kanner是Austrian-American psychiatrist，physician, and social activist。

2. 1943年 Dr. Leo Kanner首次描述该综合症为 autistic disturbance of affective contact，后来定义为 early infantile autism。

孤独症研究文章和主要推动者



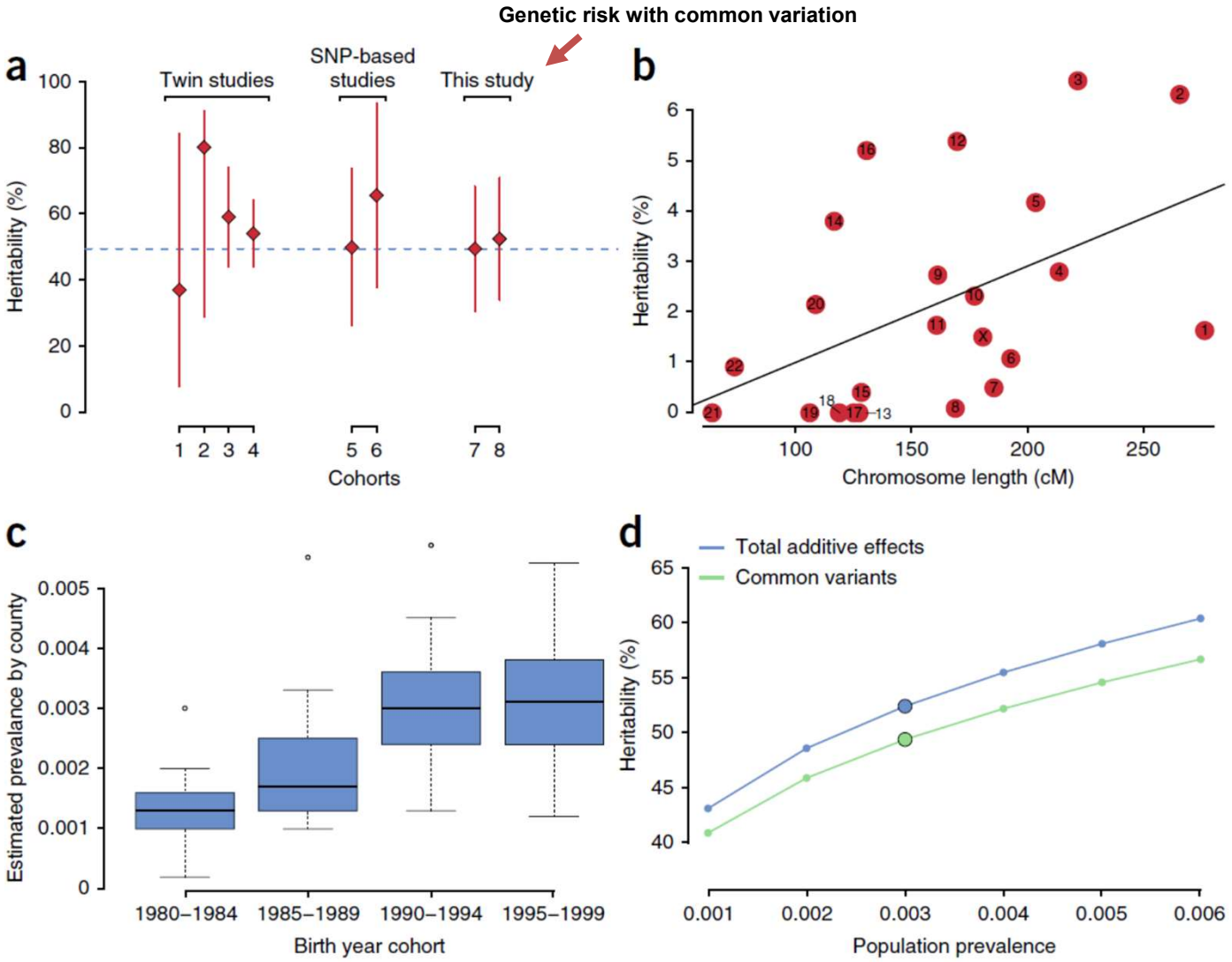
Thomas Insel

(Oct 19, 1951 –present)
Research on oxytocin and vasopressin and their impact on social behavior
NIMH Director (2002-2015)

基因缺陷和环境因素导致孤独症

遗传与孤独症

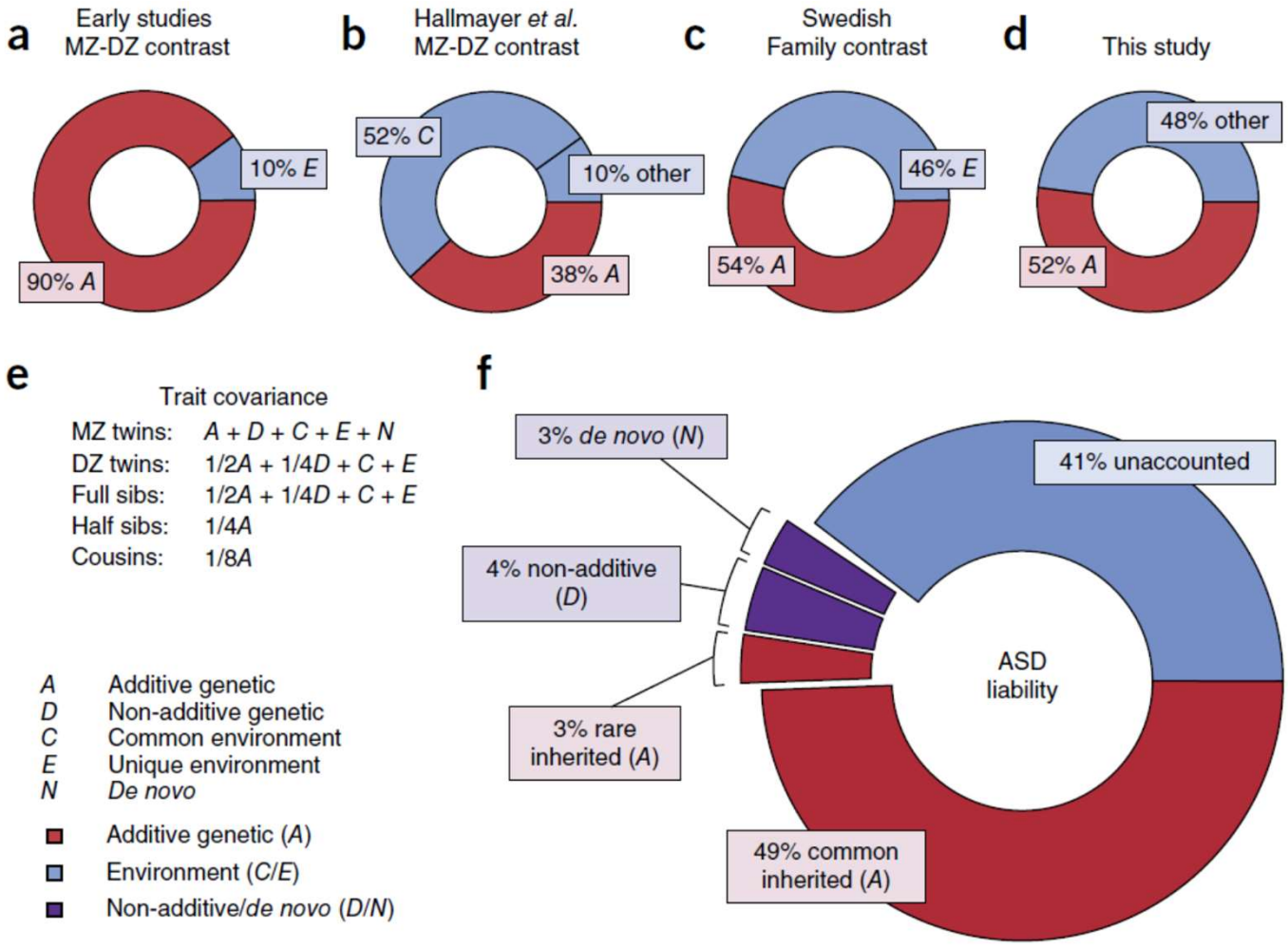
Swedish population-based autism study



Gaugler et al, *Nature Genetics* 2014

遗传和环境与孤独症

Swedish population-based autism study

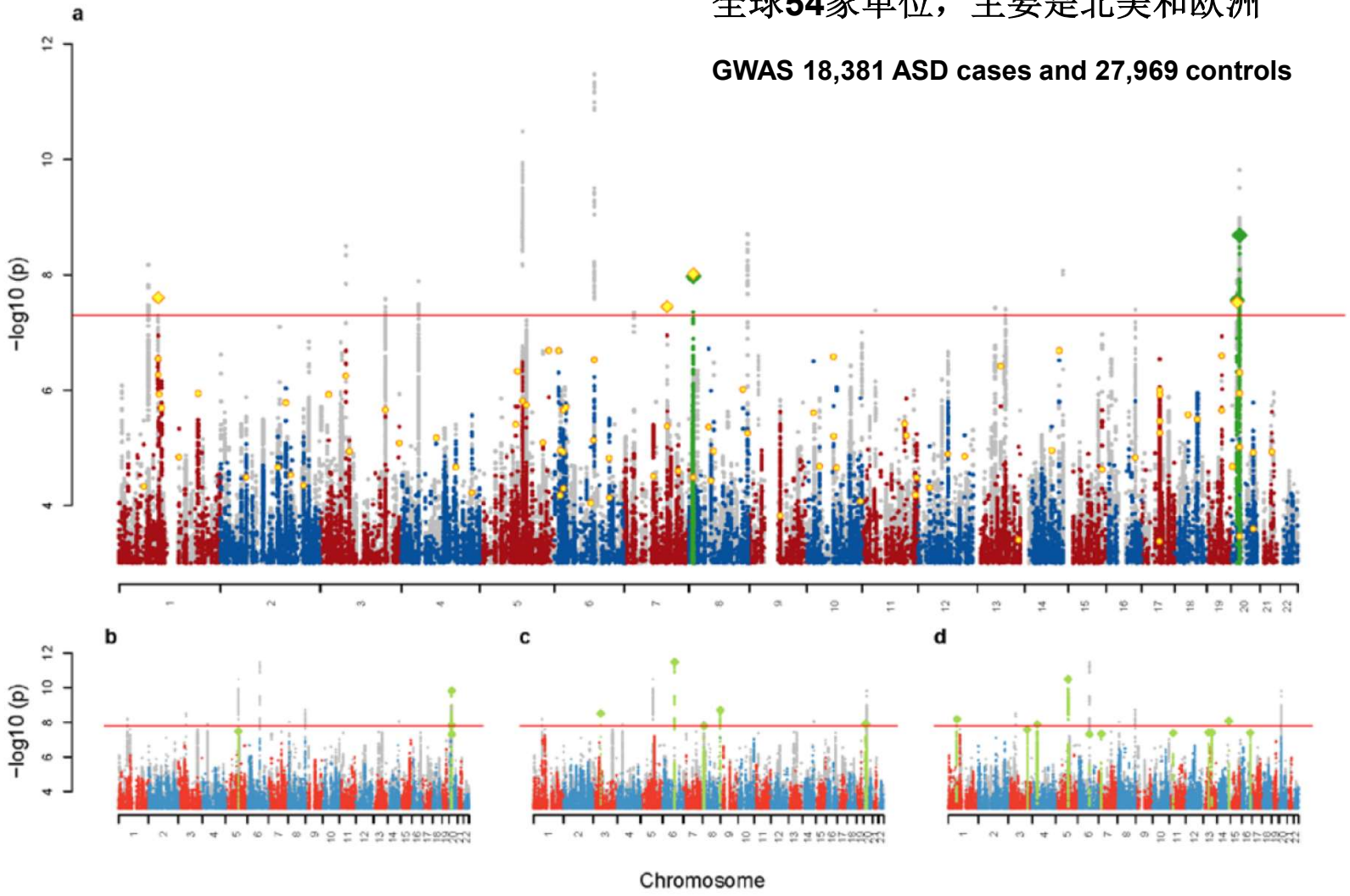


Gaugler et al, *Nature Genetics* 2014

孤独症常见风险基因组位点

全球**54**家单位，主要是北美和欧洲

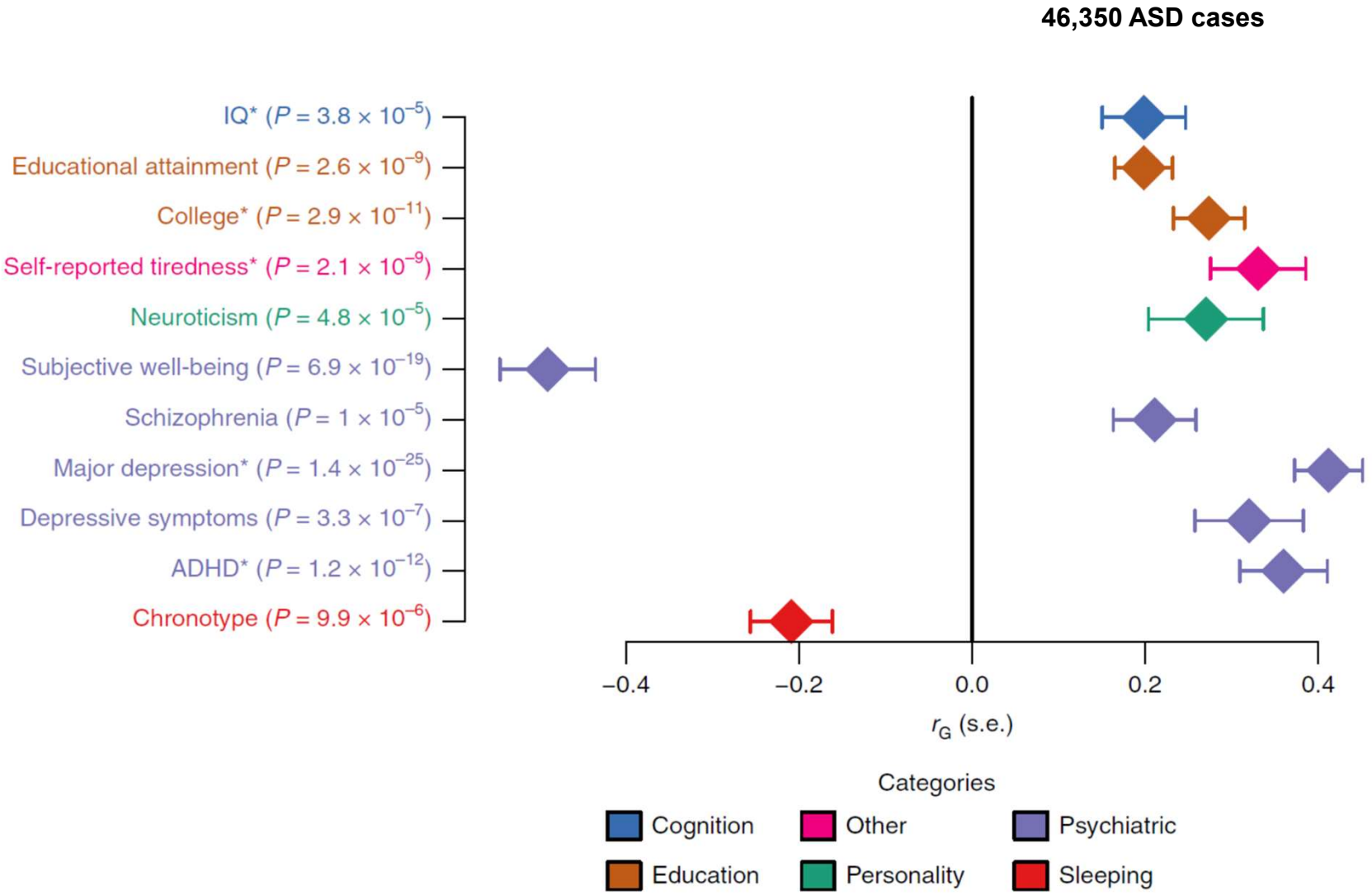
GWAS 18,381 ASD cases and 27,969 controls



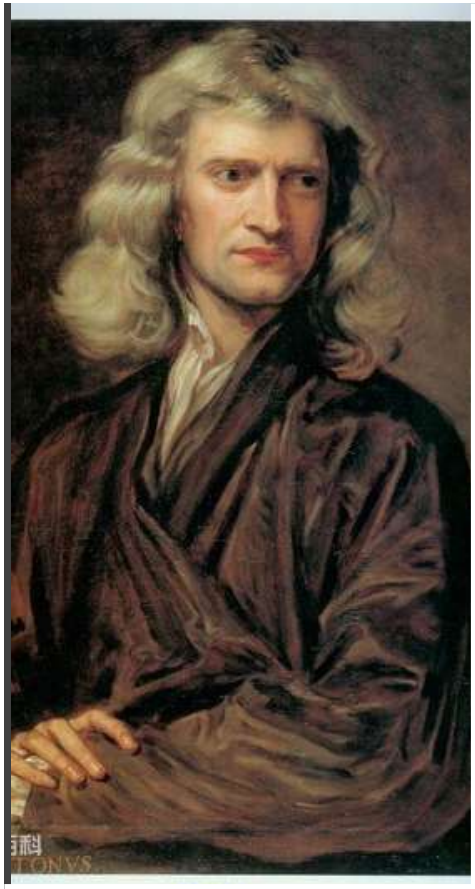
Schizophrenia **Educational Attainment** **Major Depression**

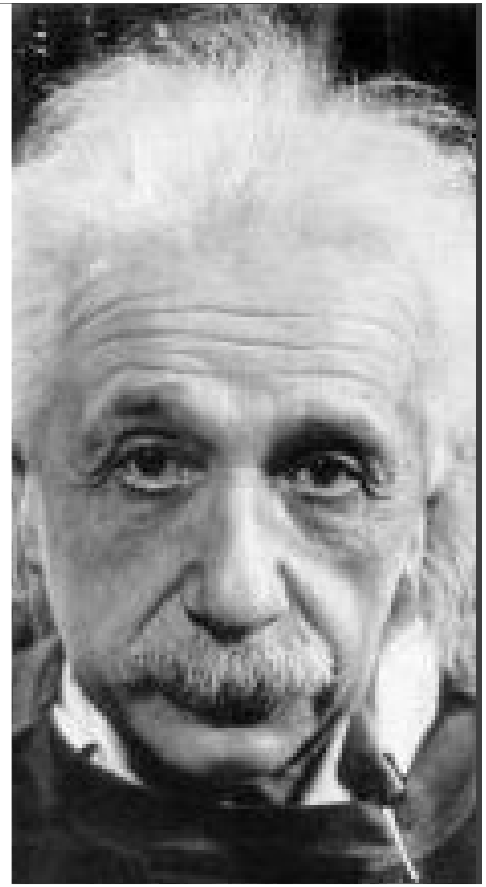
Grove et al, *Nature Genetics 2019*

孤独症遗传因素与其他性状关系



Grove et al, *Nature Genetics 2019*

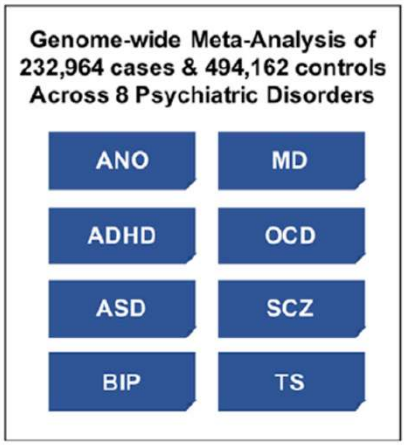


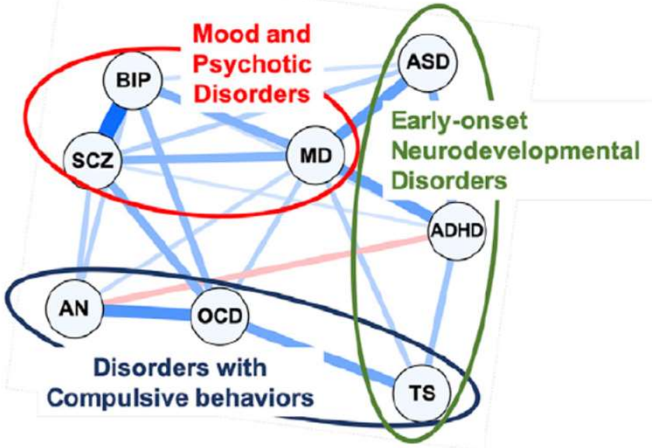
艾斯伯格症候群
(Asperger's syndrome)

人际交往困难，语言交流障碍，
刻板行为模式

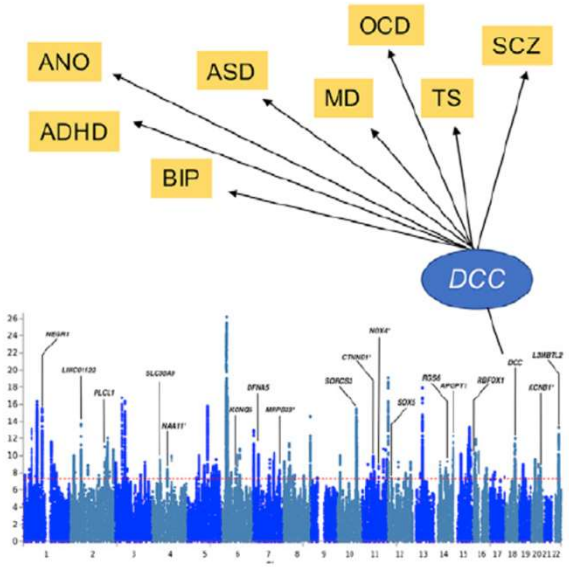
Genomic Relationships, Novel Loci, and Pleiotropic Mechanisms across Eight Psychiatric Disorders



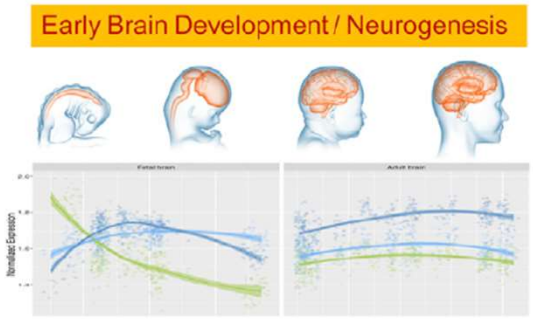
I. Substantial Genetic Correlation and Clustering

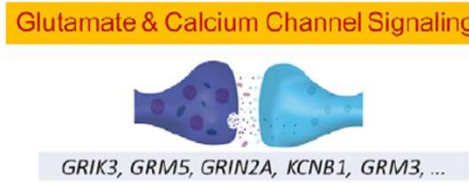


II. 109 Loci Affecting Multiple Psychiatric Disorders



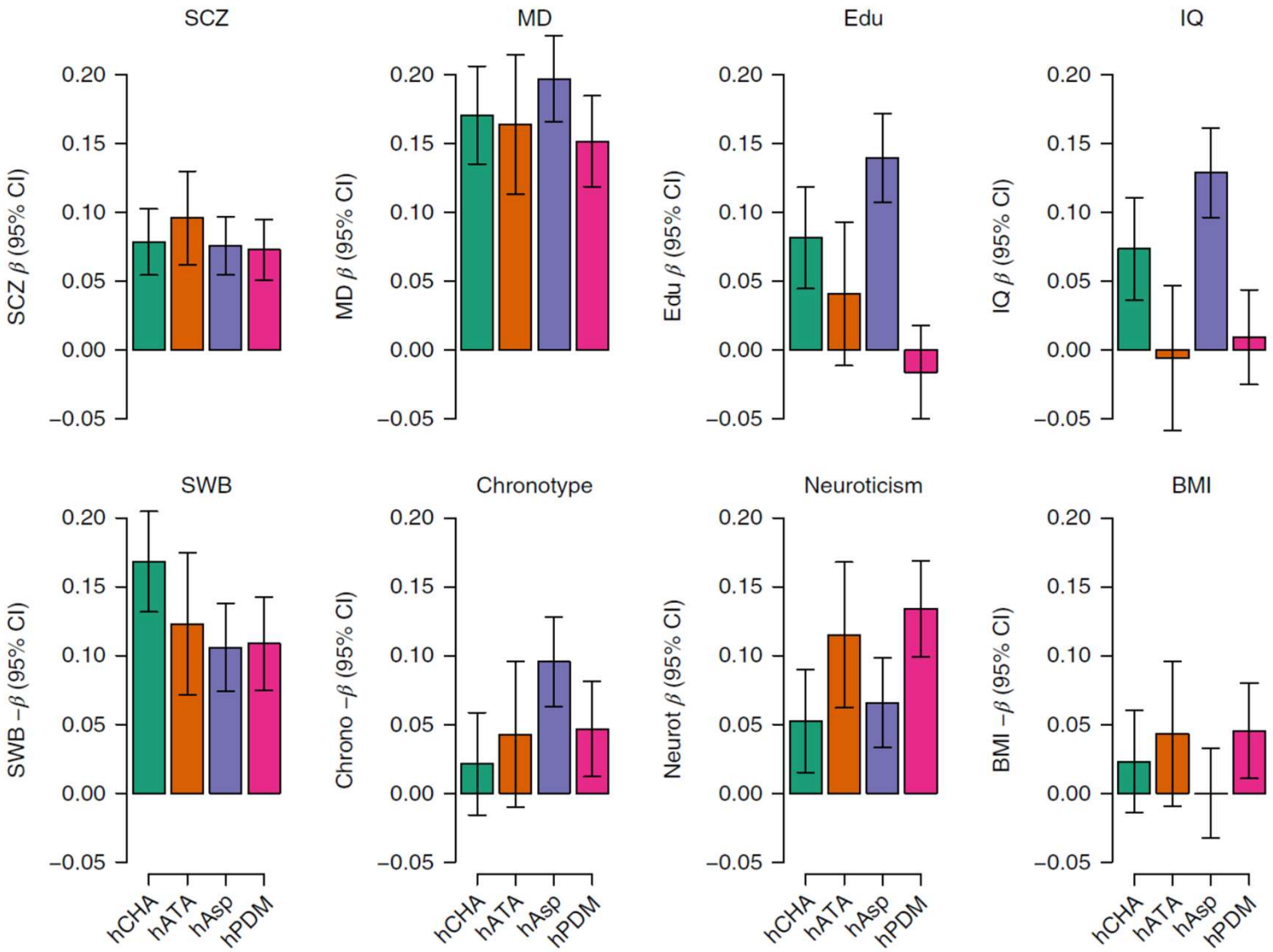
III. Gene Expression and Pathway Analyses Suggest Biological Mechanisms of Pleiotropic Loci





Cross-Disorder Group of the Psychiatric Genomics Consortium, Cell 2019

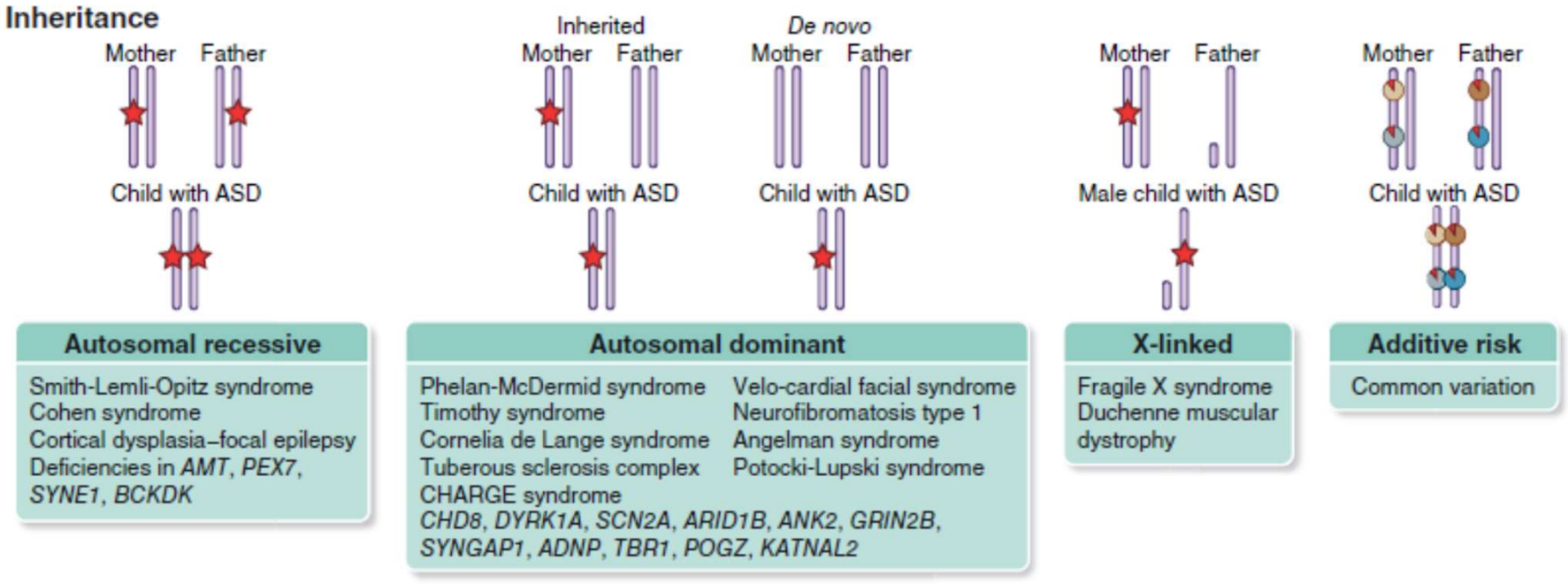
不同孤独症亚组与8种表型关系



Grove et al, *Nature Genetics 2019*

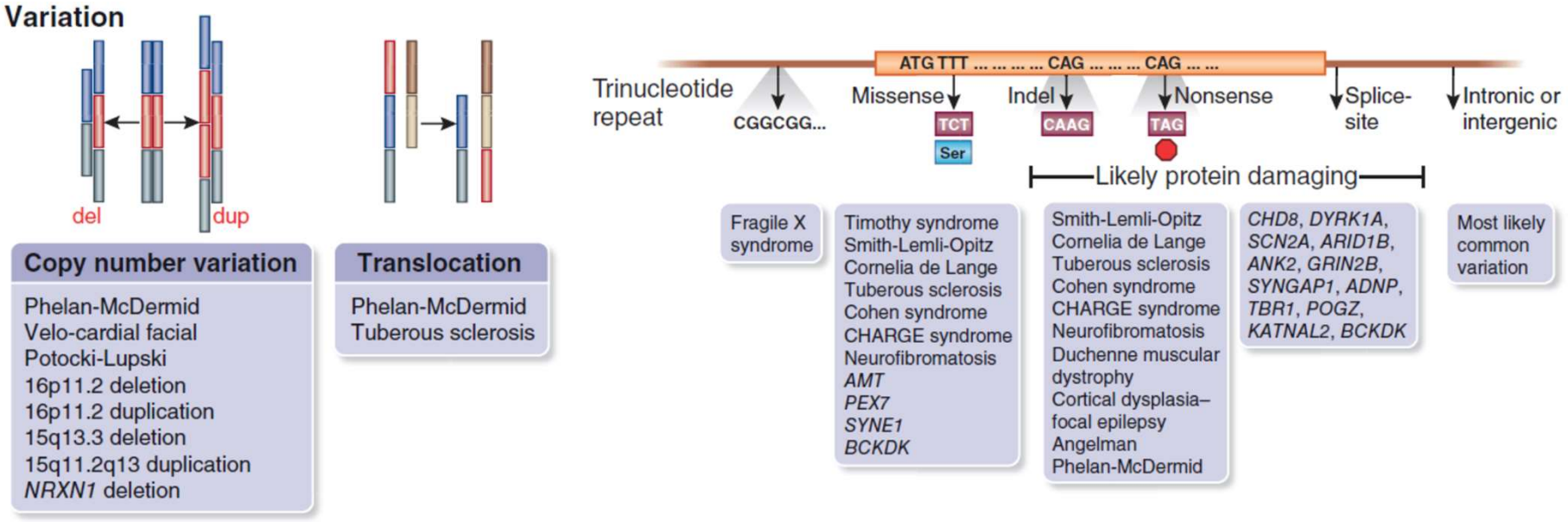
遗传与孤独症

遗传因素在孤独症发病中占**50%**左右



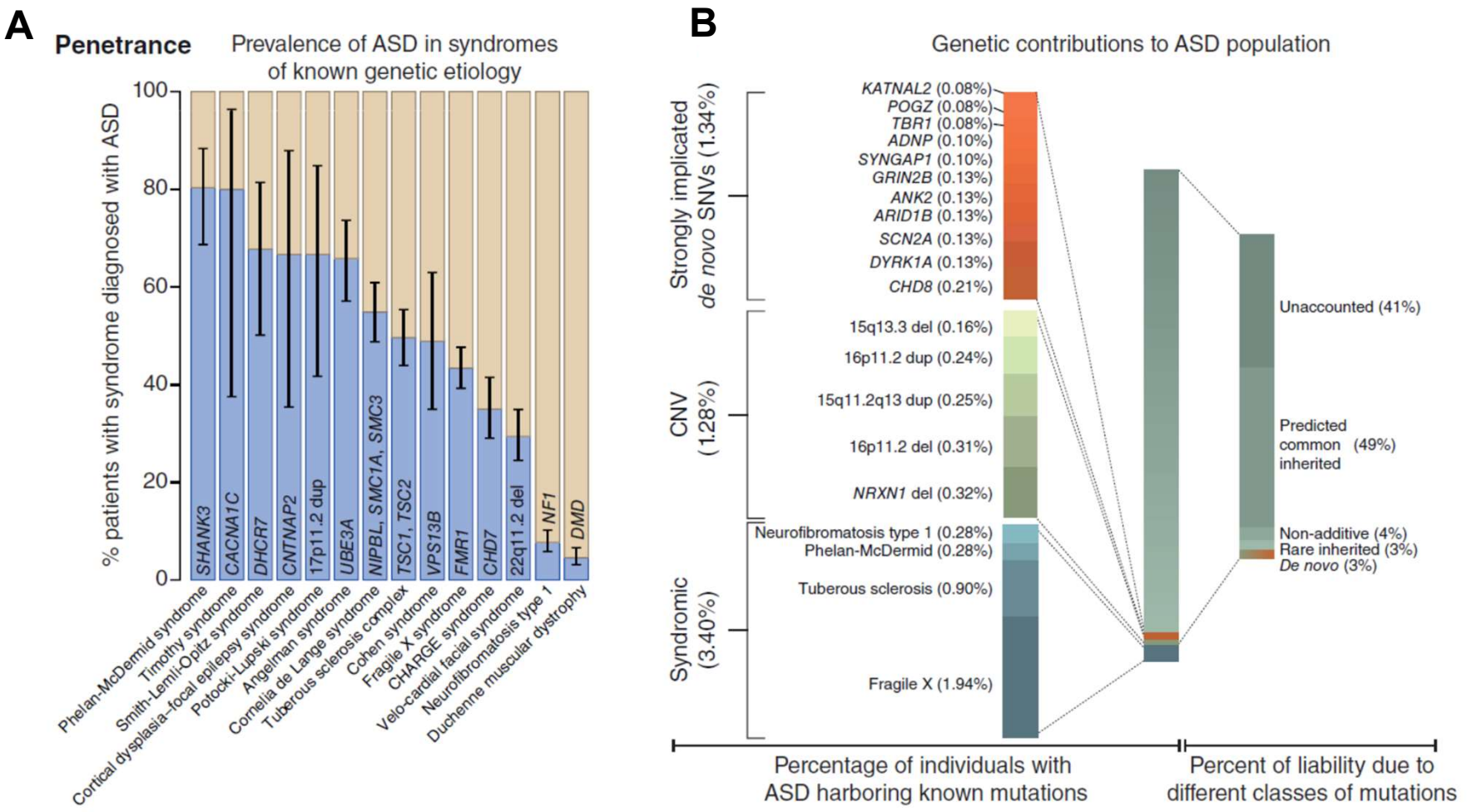
Torre-Ubieta et al, *Nature Medicine* 2016

遗传变异与孤独症



Torre-Ubieta et al, *Nature Medicine* 2016

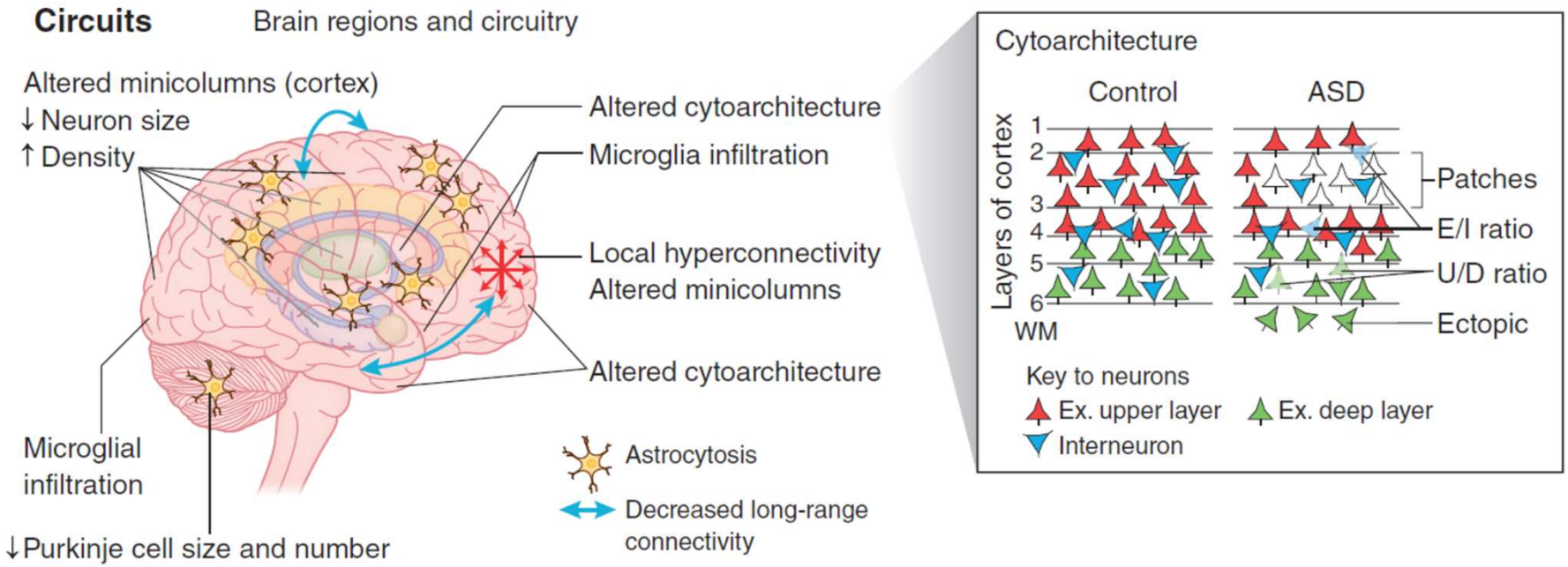
致病基因在孤独症中的遗传贡献



Torre-Ubieta et al, *Nature Medicine* 2016

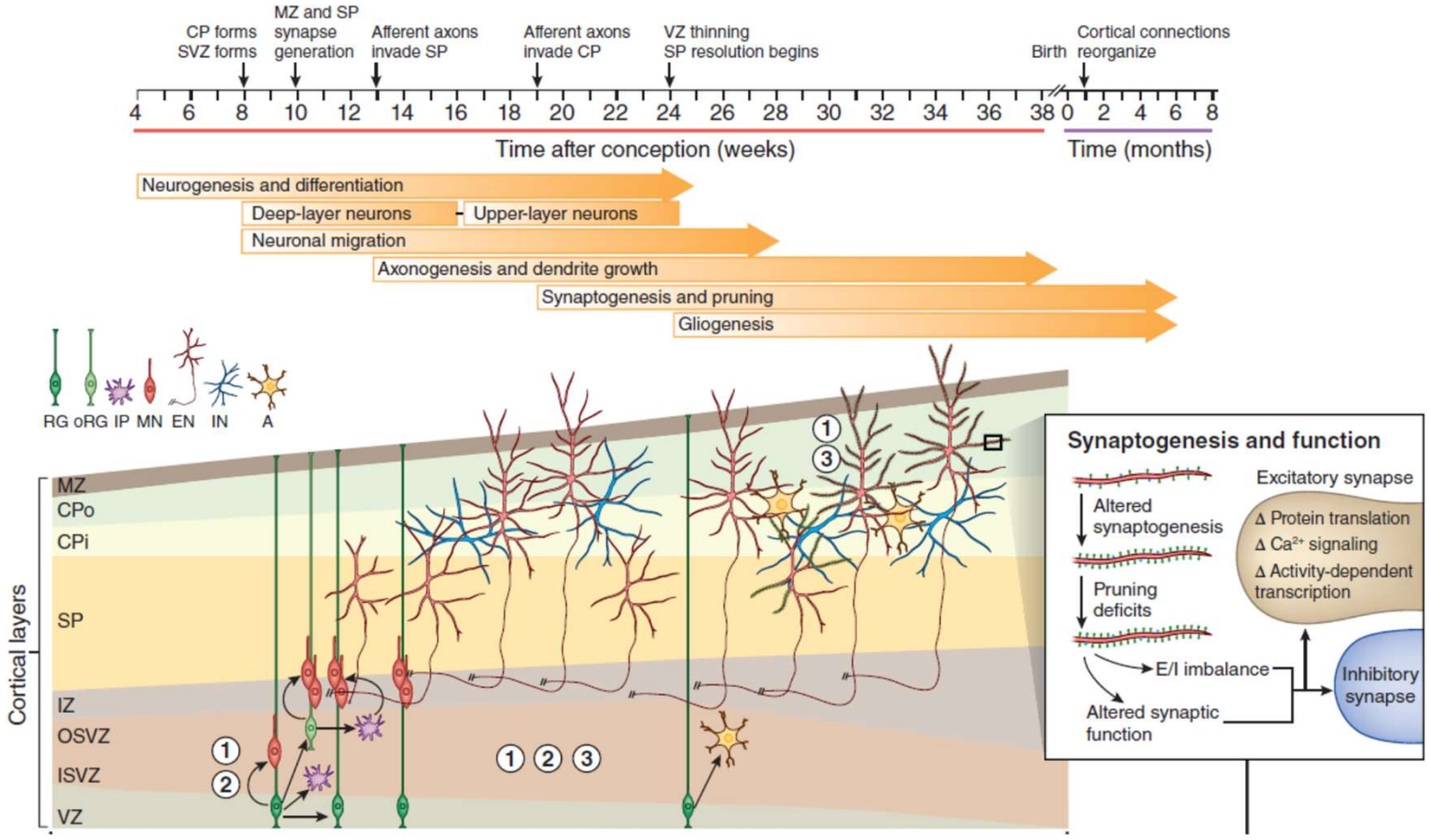
神经回路改变与孤独症

人们很早前就注意到相当比例的孤独症患儿脑体积是比正常孩子大一些，在前额叶皮层孤独症患儿的兴奋性突触连接高于正常（精神分裂症刚好相反，是低于正常），不同脑区之间的联系低于正常儿童，神经元细胞变小但密度增加，也就是说神经细胞数量增加而不是下降，小脑比较特殊-Purkinje细胞大小和数量都是下降的，可能与小胶质细胞激活造成的免疫反应有关。总体上E/I ratio失衡，兴奋性占优，所以患儿通常伴随睡眠障碍。



Torre-Ubieta et al, *Nature Medicine* 2016

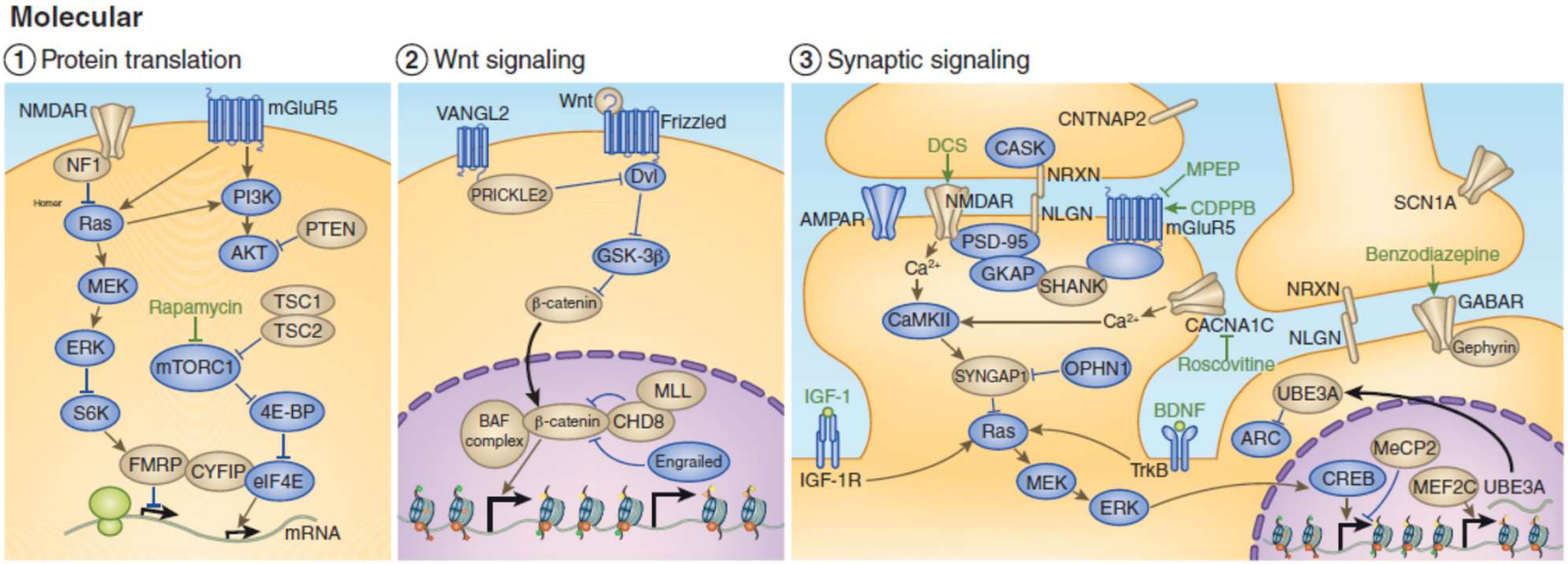
神经细胞改变与孤独症



神经回路的改变可能与基因突变导致神经细胞在发育早期迁徙出现问题有关，引起突触、树突棘发育障碍，致使脑内兴奋/抑制失衡，损害突触功能。

Torre-Ubieta et al, *Nature Medicine* 2016

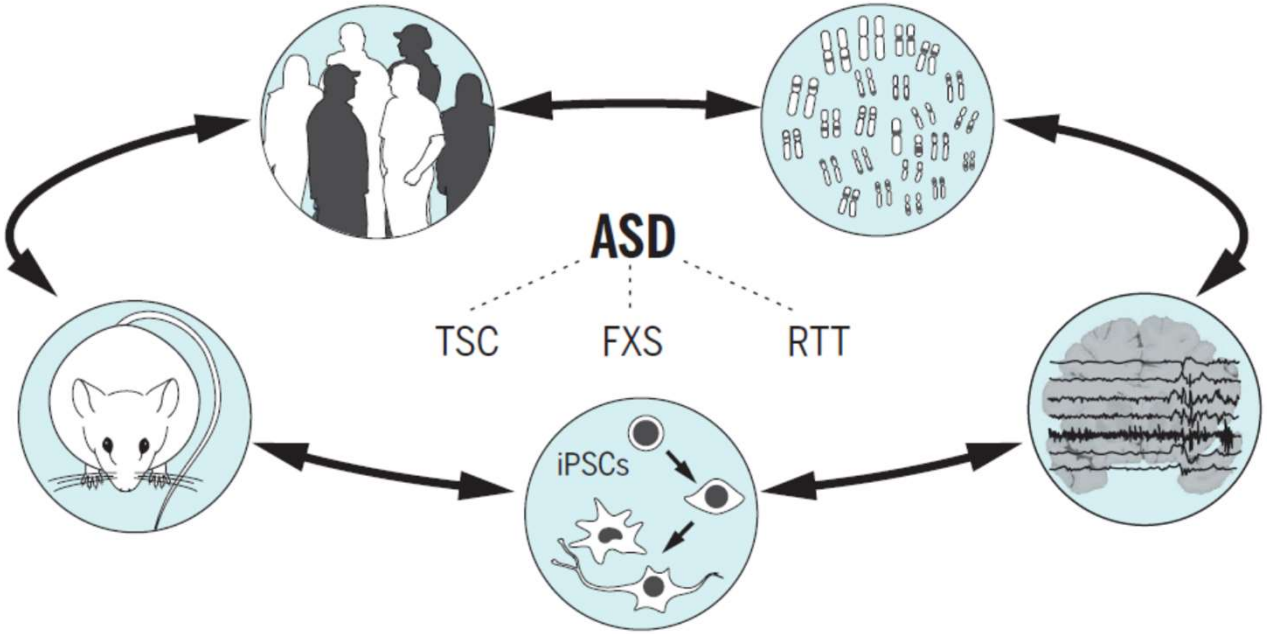
神经细胞内分子改变与孤独症



突触功能损害与神经细胞内分子改变有关，包括改变了蛋白翻译，**Wnt signaling**和 **Synaptic signaling**。

Torre-Ubieta et al, *Nature Medicine* 2016

孤独症精准治疗
转化医学研究和临床试验



由于有上百个基因突变与孤独症有关，不同患者可能是由不同的基因突变引起的，给孤独症治疗带来了相当的困难。所以，孤独症精准治疗可能是未来的方向。对孤独症基础研究、转化医学研究和临床试验就显得尤为重要。

动物模型与孤独症研究

患儿遗传学研究

转基因小鼠和猴子模型

孤独症常见突变基因及动物模型

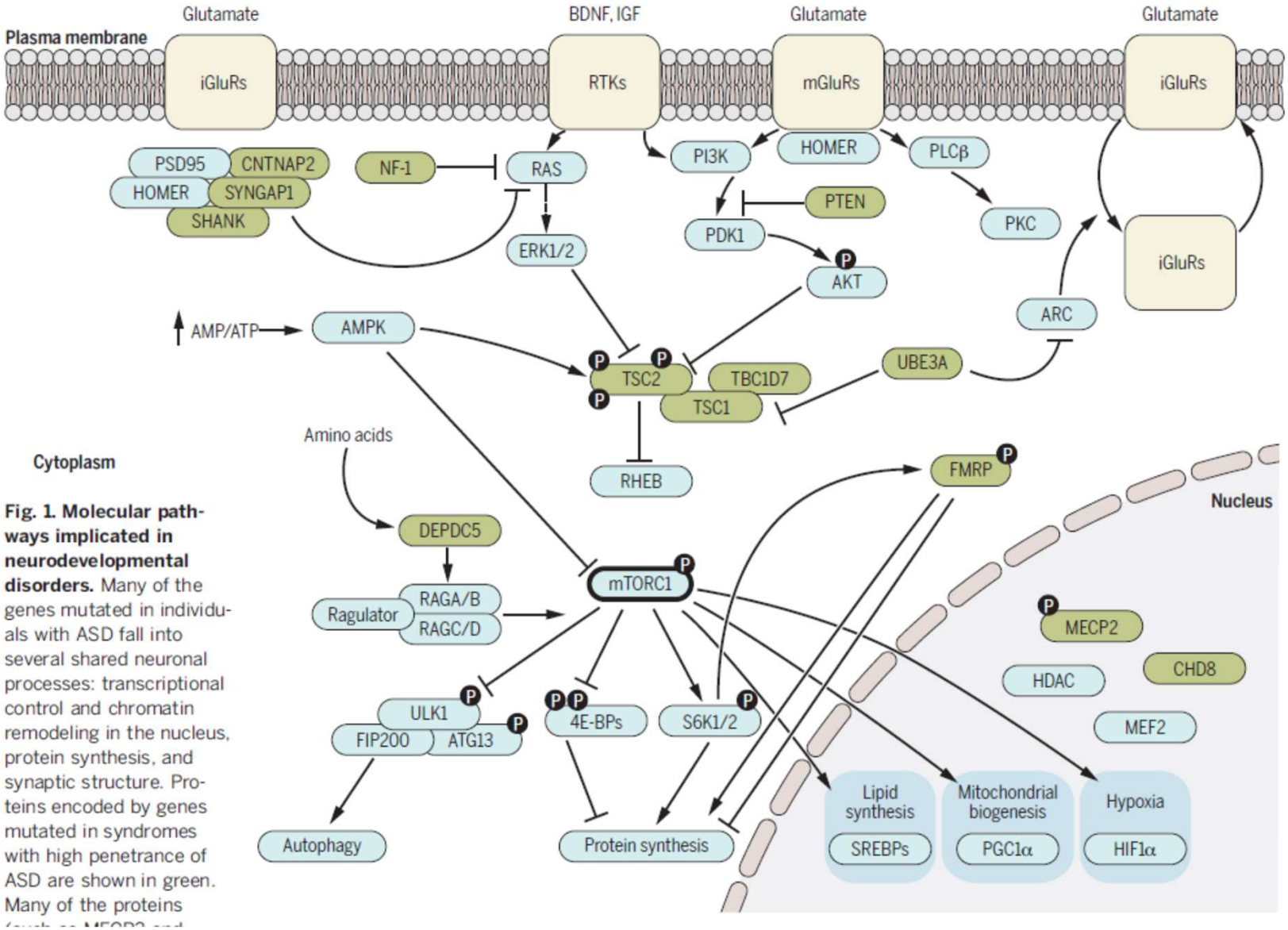


Fig. 1. Molecular pathways implicated in neurodevelopmental disorders. Many of the genes mutated in individuals with ASD fall into several shared neuronal processes: transcriptional control and chromatin remodeling in the nucleus, protein synthesis, and synaptic structure. Proteins encoded by genes mutated in syndromes with high penetrance of ASD are shown in green. Many of the proteins

导致孤独症的神经生物学机理

Brain region and mechanism	Supporting evidence	Caveats and limitations	Treatment potential
Neocortex			
Brain overgrowth	• Multiple studies with large cohorts measuring brain size (MRI) and head circumference • Mutations in genes controlling neurogenesis and growth (**Fig. 2**)	• Small effect size (2 mm) • Potential bias in measurements • Incomplete understanding of biological mechanism. Evidence for both white and gray matter origin	• Limited. Targeting key pathways potentially risks broad developmental problems • Rapamycin treatment reversed macrocephaly in a mouse model[184]
Altered cortical cytoarchitecture (neuron size, number, positioning and/or orientation)	• Cumulative evidence from >12 neuropathological studies • Mutations in genes controlling neurogenesis, growth and neuronal migration (**Fig. 2**) • Modeling in mice consistent with observed phenotypes (**Table 1**)	• Small cohorts. No systematic assessment of the same brain regions and phenotypes • Multiple phenotypes; none unique to ASD	• Limited. Targeting key pathways potentially risks broad developmental problems
Neuronal morphogenesis	• White matter reduction in neuropathological studies. Narrow minicolumns and altered connectivity in cortical circuits • Mutations in genes controlling axon growth or guidance and dendrite arborization (**Fig. 2**)	• Small cohorts. Limited number of studies	• Limited. Targeting key pathways will probably lead to broad developmental problems • Rapamycin successfully used in rescue experiments in mice[184,240]
Synaptogenesis	• Increased layer-specific dendritic spine density in frontal (L2), parietal (L2) and temporal lobes (L2, L5)[144,145] • Mutations in genes converge in pathways regulating synaptogenesis (**Fig. 2**) • Increased spines and upregulated spine dynamics in some mouse models[192,193,283]	• Only two studies with small cohorts[144,145] • Unclear mechanism: both increase and decrease in synapse density reported in mouse models (**Table 1**)	• Promising. Phenotypic reversal possible in postnatal periods • IGF1 successfully used in rescue experiments in hiPSC[100,102] • PI3K antagonists rescue FXS-associated increased spine density in mice[271]
Synaptic dysfunction E/I imbalance	• Decreased GABA receptor density and altered GAD1 and GAD2 levels. Functional imaging studies identify local hyperconnectivity and decreased long-range connections • Mutations in genes converge in pathways regulating synaptic function (**Fig. 2**) • Mouse models support disruption in E/I balance leads to ASD phenotypes (**Table 1**). Increasing E/I in prefrontal cortex using optogenetics leads to social deficits[157]	• Poorly documented in neuropathological studies. Small cohorts • Unclear mechanism: both increase and decrease in excitatory synaptic function reported with and without concomitant inhibitory compensation. Multiple molecular mechanisms leading to synaptic dysfunction, including altered translation, Ca^{2+} signaling and activity-dependent transcription (**Fig. 2**)	• Promising. Phenotypic reversal possible in postnatal periods • IGF1 rescues phenotypes in mouse models and hiPSC[100,102,177] • Positive allosteric modulators for $GABA_A$ receptor[239], mGluR5 antagonists and agonists[230,232,233], NMDAR partial agonist[170,232], and blockers of NKCC1 cation-chloride cotransporter[251] restored behavioral deficits in mice
Cerebellum			
Purkinje cell (PC) loss and dysfunction	• Reported decrease in PC size and number. Motor coordination problems in ASD • PC-specific ablation of ASD risk gene *Tsc1* in mice recapitulates core ASD phenotypes and PC degeneration[183] • Developmental cerebellar injury increases ASD risk[206]	• Small cohorts. Limited number of studies. Gliosis observed in most • Global gene expression profiles between cerebellums of control subjects and those with ASD very similar[89] • Limited knowledge of the role of the cerebellum in ASD behavioral domains	• Promising. Postnatal cerebellar development increases therapeutic potential • Rapamycin successfully used in rescue experiments in mice[183]
Widespread			
Neuron-glia signaling	• Reported increased microglia infiltration and astrogliosis in multiple brain regions (neuropathology and PET imaging) • Post-mortem transcriptome identifies increased microglial and immune signature[89,223] • Role of microglia and astrocytes in regulating synapse formation, function and pruning. Disrupted neuron-microglia signaling in mice leads to social deficits[225]	• Small cohorts. Limited number of studies • Lack of genetic evidence suggests a reactive role • Limited characterization in ASD mouse models	• Untested, but promising • Microglia- and astrocyte-specific rescue experiments in Rett mouse models rescues disease phenotypes[284,285]

ARTICLES
https://doi.org/10.1038/s41593-018-0110-8

nature neuroscience

Corrected: Publisher Correction

Social deficits in *Shank3*-deficient mouse models of autism are rescued by histone deacetylase (HDAC) inhibition

Luye Qin[1], Kaijie Ma[1], Zi-Jun Wang[1], Zihua Hu[2], Emmanuel Matas[1], Jing Wei[1] and Zhen Yan[1*]

Haploinsufficiency of the *SHANK3* gene is causally linked to autism spectrum disorder (ASD), and ASD-associated genes are also enriched for chromatin remodelers. Here we found that brief treatment with romidepsin, a highly potent class I histone deacetylase (HDAC) inhibitor, alleviated social deficits in *Shank3*-deficient mice, which persisted for ~3 weeks. *HDAC2* transcription was upregulated in these mice, and knockdown of *HDAC2* in prefrontal cortex also rescued their social deficits. Nuclear localization of β-catenin, a Shank3-binding protein that regulates cell adhesion and transcription, was increased in *Shank3*-deficient mice, which induced *HDAC2* upregulation and social deficits. At the downstream molecular level, romidepsin treatment elevated the expression and histone acetylation of *Grin2a* and actin-regulatory genes and restored NMDA-receptor function and actin filaments in *Shank3*-deficient mice. Taken together, these findings highlight an epigenetic mechanism underlying social deficits linked to *Shank3* deficiency, which may suggest potential therapeutic strategies for ASD patients bearing *SHANK3* mutations.

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22q13.3 deletion syndrome
Phelan-McDermid syndrome

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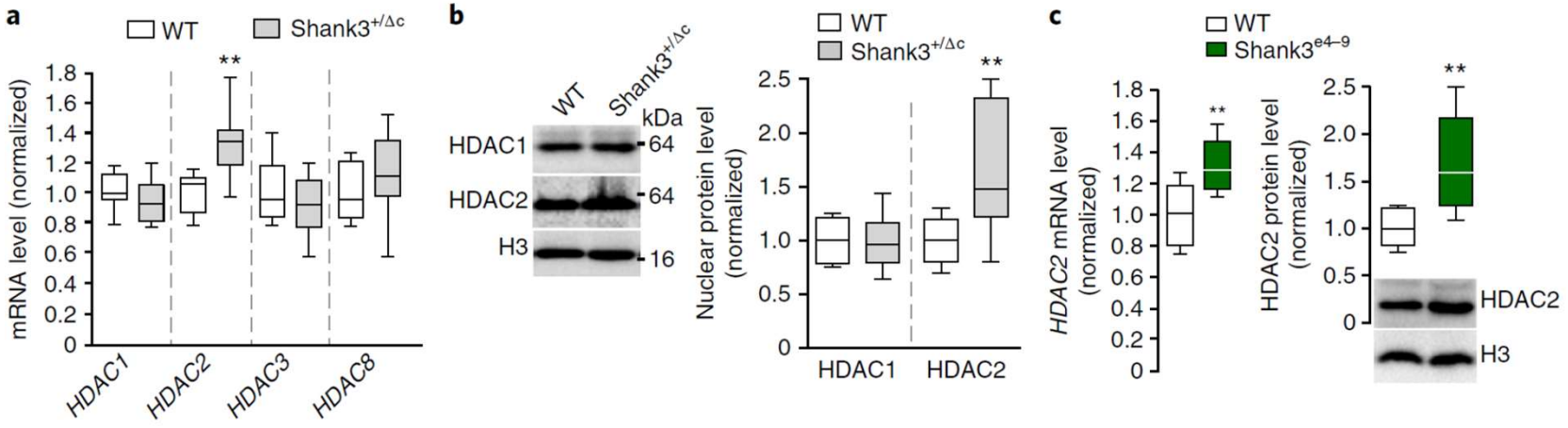
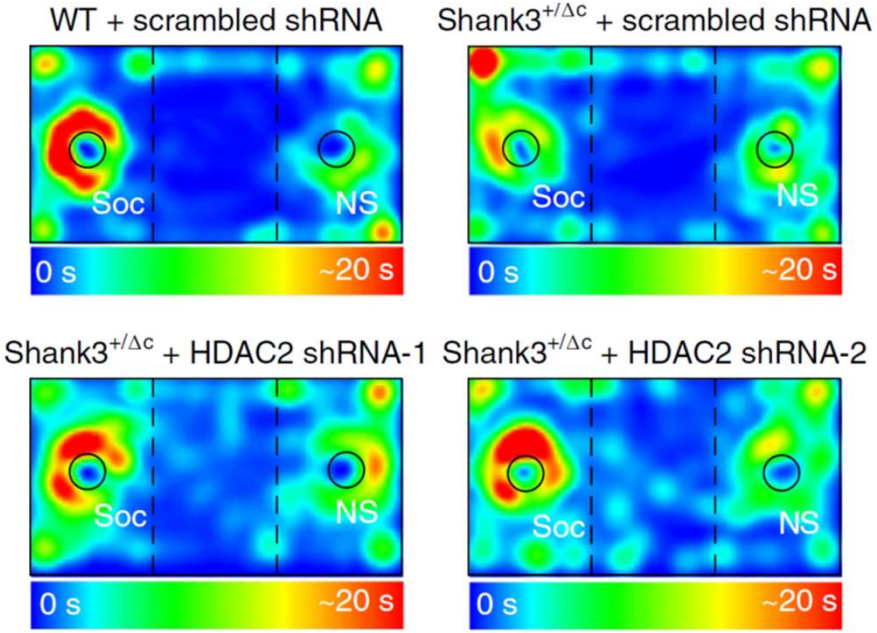
这个工作主要是研究**Shank3**缺失对动物社交行为的影响，以及用什么药物能够改善动物社交活动。

Shank3 缺失引起前额叶HDAC2 升调, Knockdown HDAC2过量表达，能够改善由于Shank3缺失导致的动物社交活动障碍。



Three-chamber sociability tests

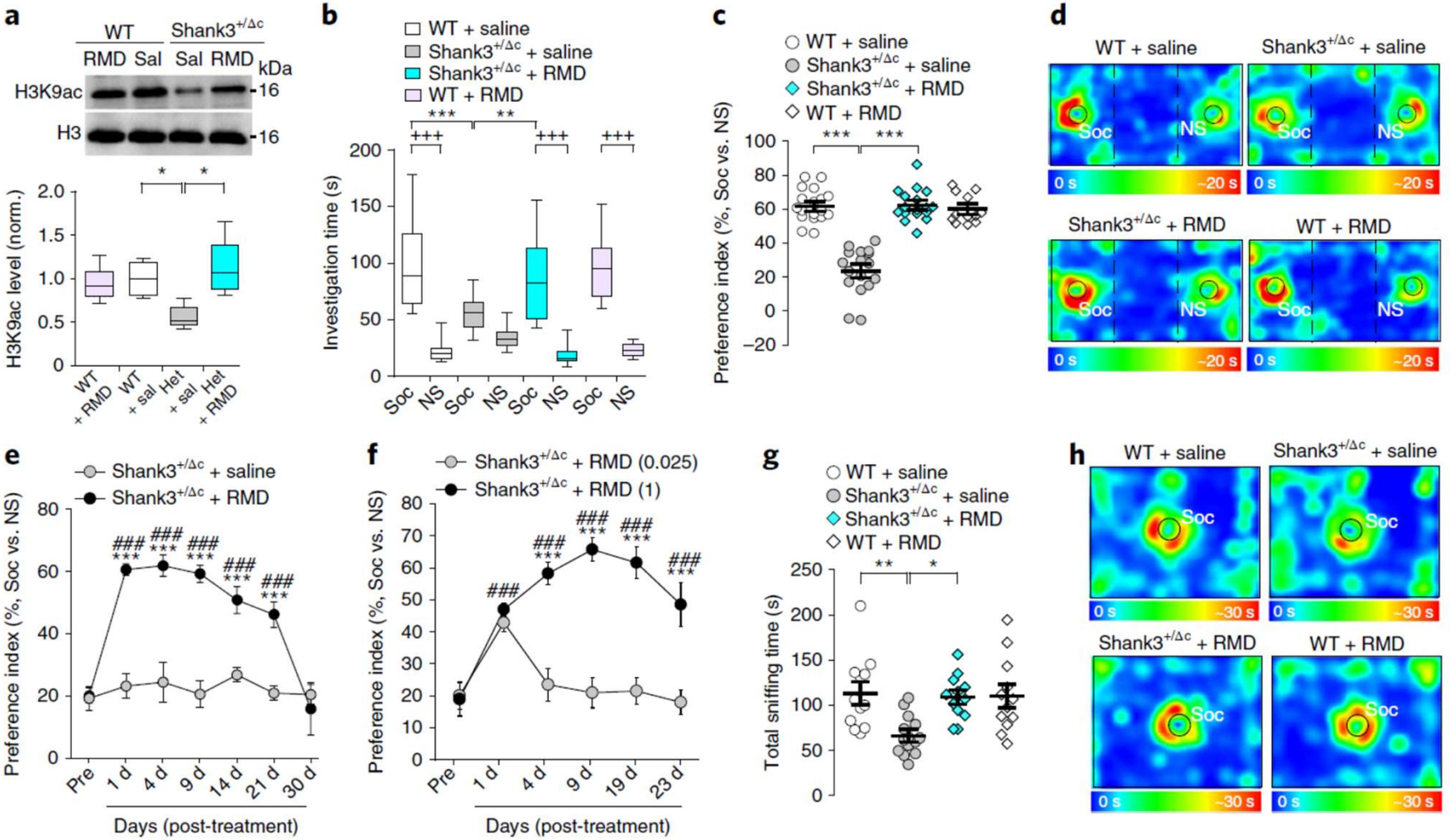


Shank3 KO 小鼠有明显的社交活动障碍，在前额叶皮层中微量注射**HDAC2 shRNA-1** 和 **HDAC2 shRNA-2**，减少**HDAC2**过量表达，能够改善由于**Shank3**缺失导致的动物社交活动障碍。

Qin et al, *Nature Neuroscience* 2018

HDAC 抑制剂 Romidepsin 长时间地改善动物自闭症样的行为障碍

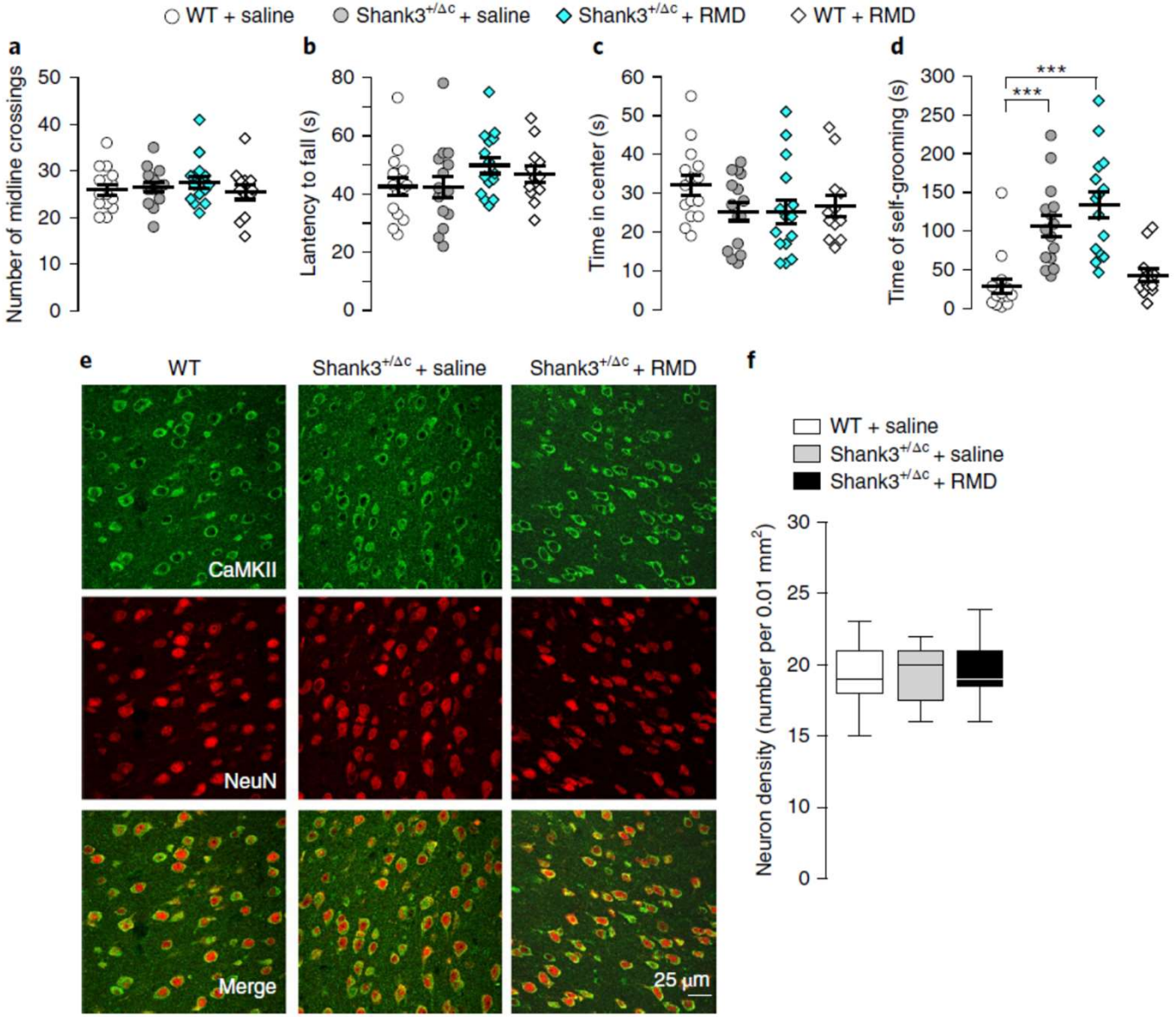
Romidepsin是美国FDA批准治疗癌症的药物。Romidepsin通过抑制HDAC来增加皮层acetylated H3 表达，从而改善动物的行为。



连续3天腹腔注射（0.25mg/kg），对动物行为改善可达3周。而且这种改善效应呈现剂量依赖性。

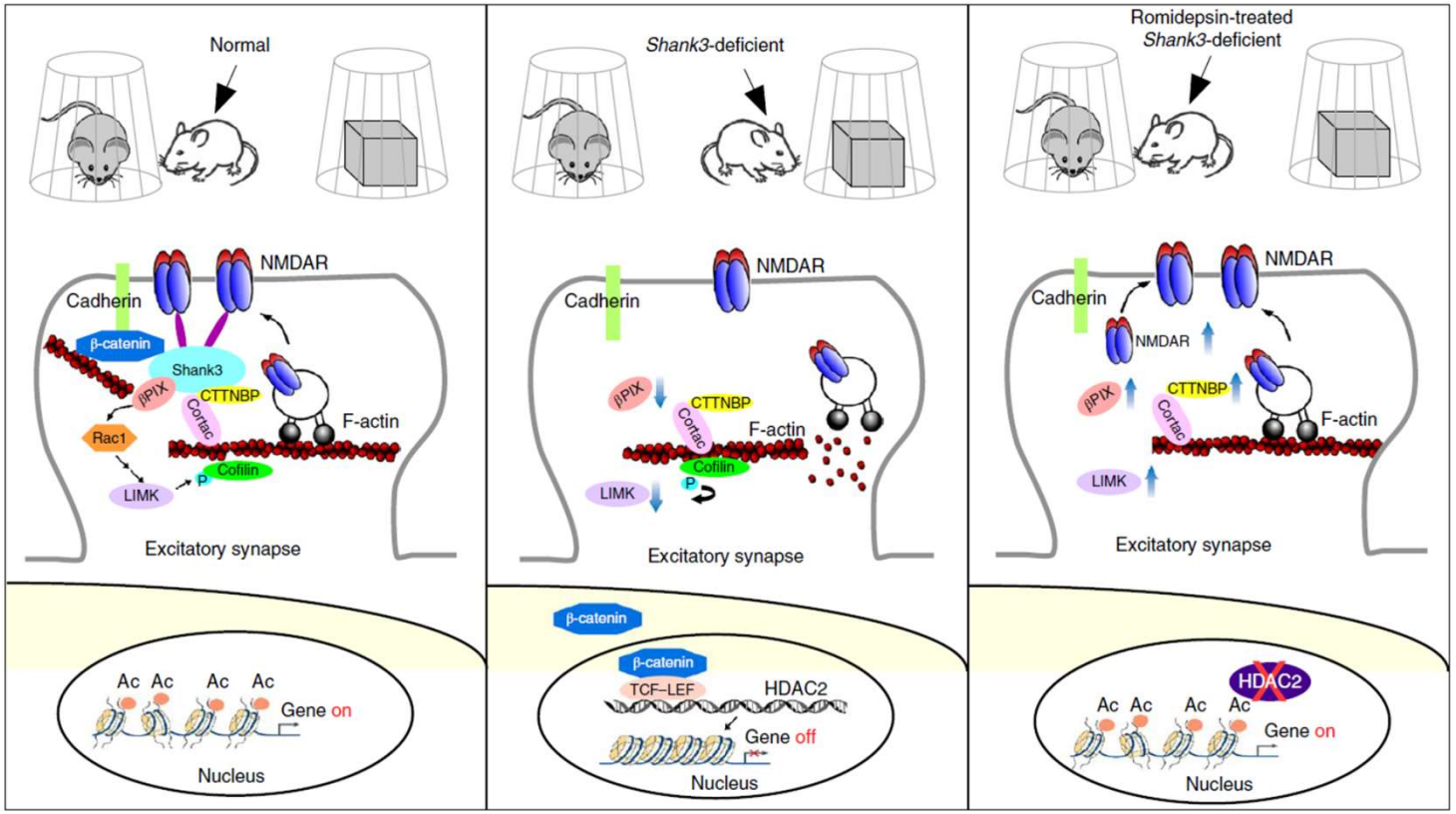
Qin et al, Nature Neuroscience 2018

Romidepsin并不影响动物的运动、焦虑症样行为，也不影响皮层第五层锥体神经元成活，但也不能够改善动物的重复刻板活动。



Qin et al, Nature Neuroscience 2018

Romidepsin修复Shank3缺失导致的社交障碍



正常功能的Shank3在维持突触后膜NMDA受体表达起重要作用，当Shank3缺失造成HDAC2表达增加，引起细胞核内基因包括NMDA基因表达下降，致使突触后膜上的NMDA受体表达下降，造成突触功能障碍，引起动物的孤独症样的行为学改变。当抑制了HDAC2后，这个过程就反过来了，核内基因表达增加、包括NMDA表达增加，改善突触传递功能和动物的孤独症行为。

Qin et al, *Nature Neuroscience* 2018

ARTICLE

https://doi.org/10.1038/s41586-018-0416-4

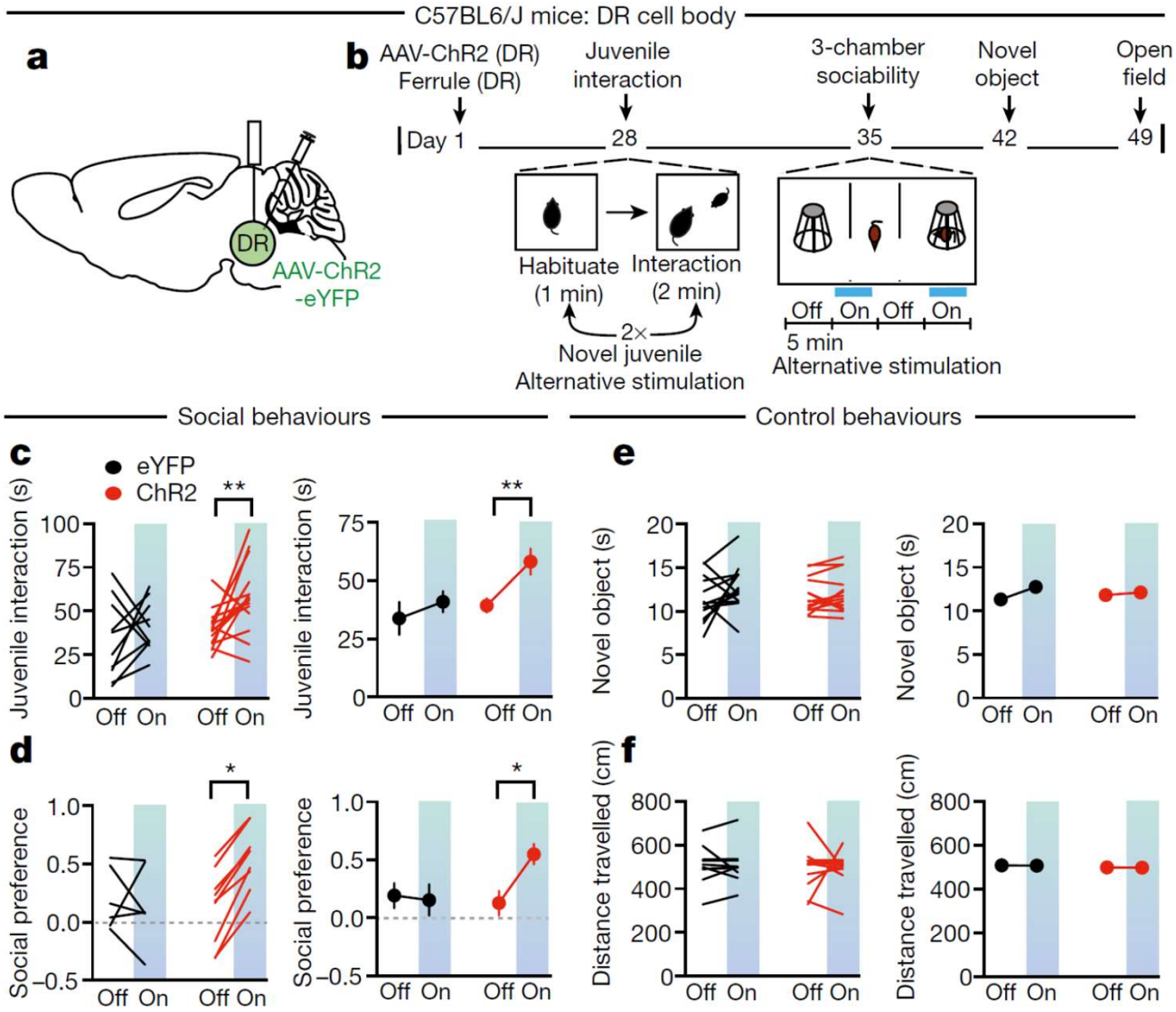
5-HT release in nucleus accumbens rescues social deficits in mouse autism model

Jessica J. Walsh[1], Daniel J. Christoffel[1], Boris D. Heifets[2], Gabriel A. Ben-Dor[1], Aslihan Selimbeyoglu[1,3,4], Lin W. Hung[1], Karl Deisseroth[3,4] & Robert C. Malenka[1]*

Dysfunction in prosocial interactions is a core symptom of autism spectrum disorder. However, the neural mechanisms that underlie sociability are poorly understood, limiting the rational development of therapies to treat social deficits. Here we show in mice that bidirectional modulation of the release of serotonin (5-HT) from dorsal raphe neurons in the nucleus accumbens bidirectionally modifies sociability. In a mouse model of a common genetic cause of autism spectrum disorder—a copy number variation on chromosome 16p11.2—genetic deletion of the syntenic region from 5-HT neurons induces deficits in social behaviour and decreases dorsal raphe 5-HT neuronal activity. These sociability deficits can be rescued by optogenetic activation of dorsal raphe 5-HT neurons, an effect requiring and mimicked by activation of 5-HT1b receptors in the nucleus accumbens. These results demonstrate an unexpected role for 5-HT action in the nucleus accumbens in social behaviours, and suggest that targeting this mechanism may prove therapeutically beneficial.

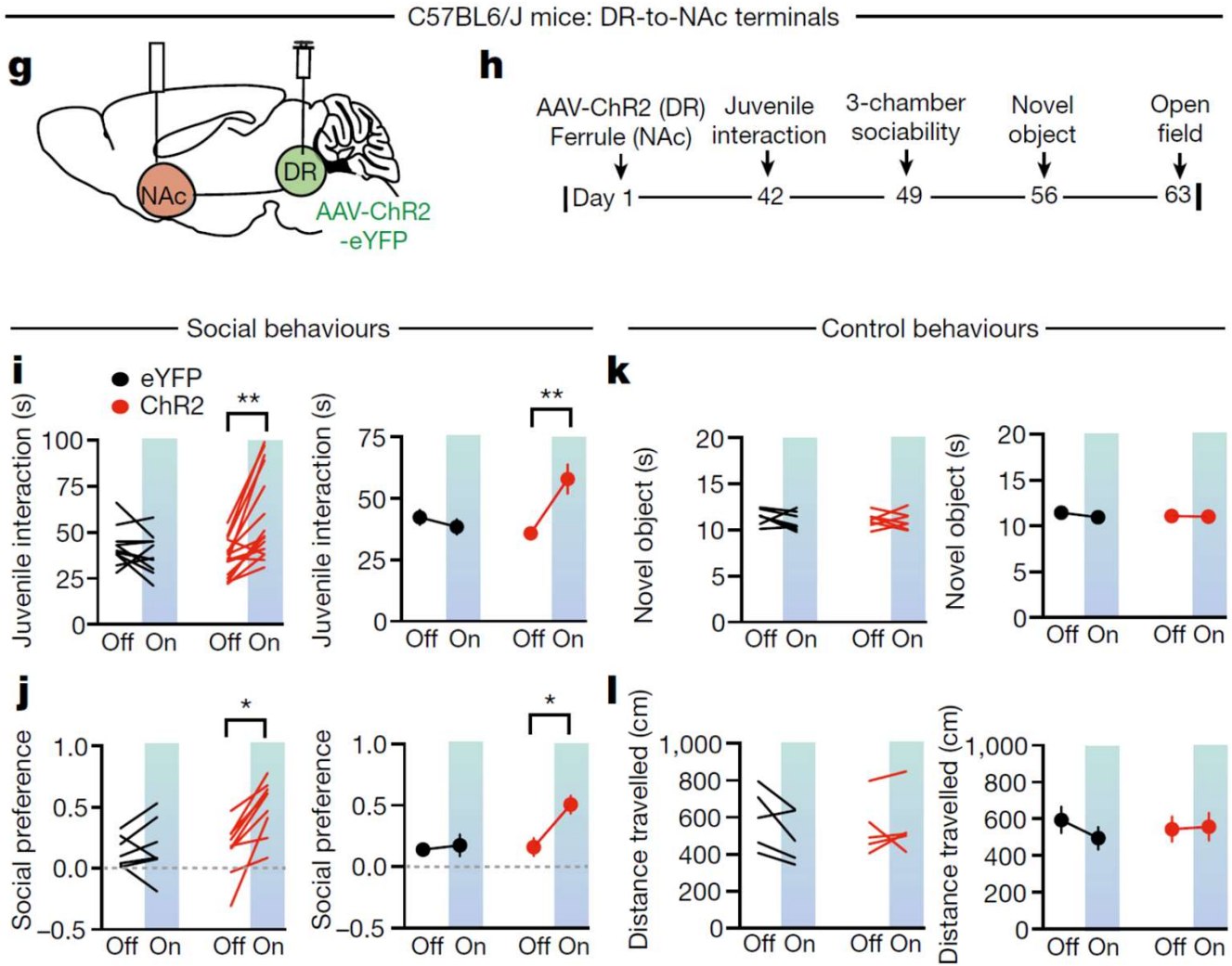
16p11.2 deletion syndrome也归属于ASD。增加5-HT在伏核（nucleus accumbens）释放，能够改善相对应16p11.2缺失的小鼠孤独症模型的行为缺失。

刺激中缝核的神经元能够增加动物社交活动



Walsh et al, Nature 2018

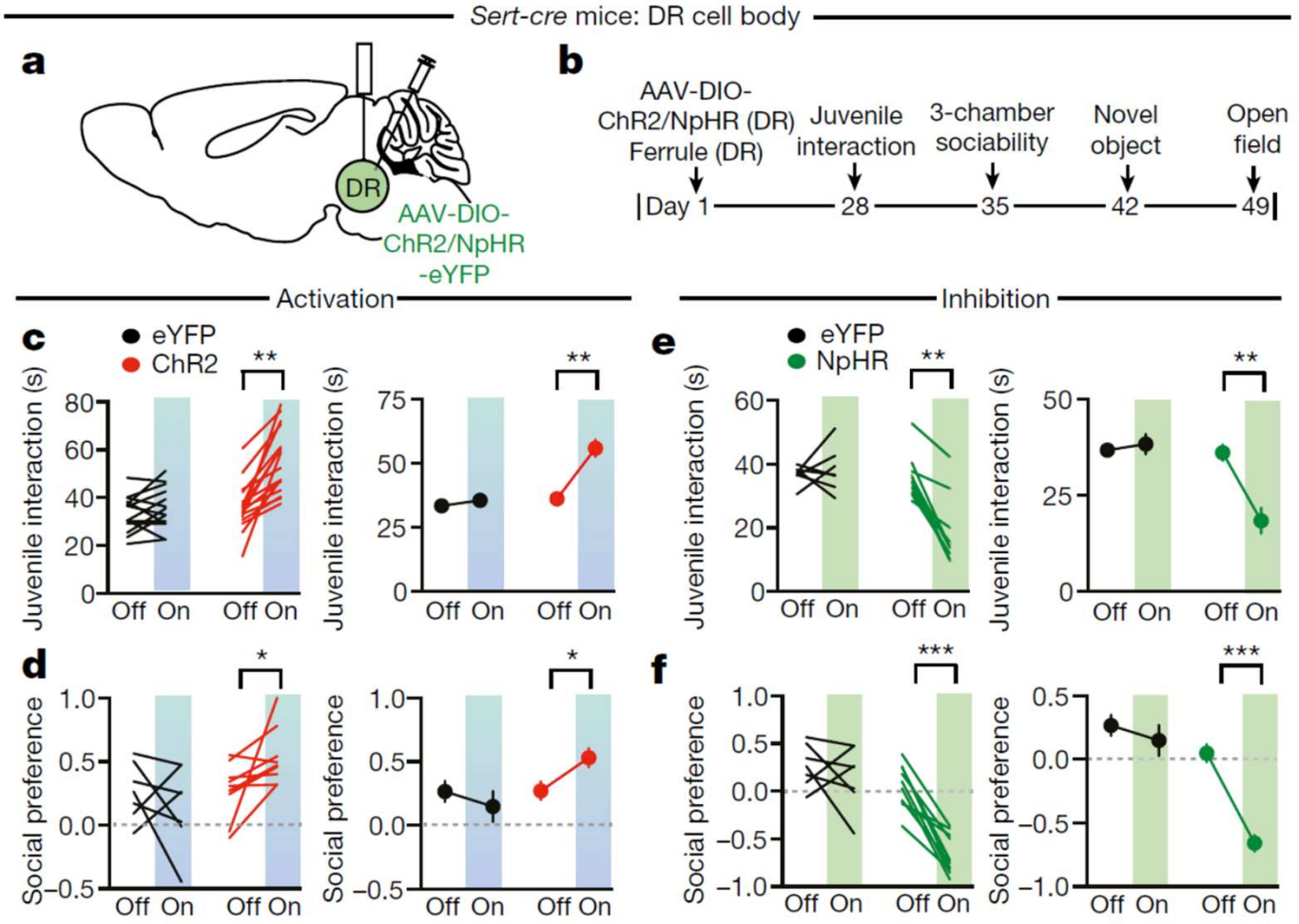
刺激中缝核-伏核5-HT通路增加动物社交活动



提示中缝核-伏核5-HT通路在动物社交活动中起作用。

Walsh et al, Nature 2018

中缝核5-HT神经元对社交活动的双向调节

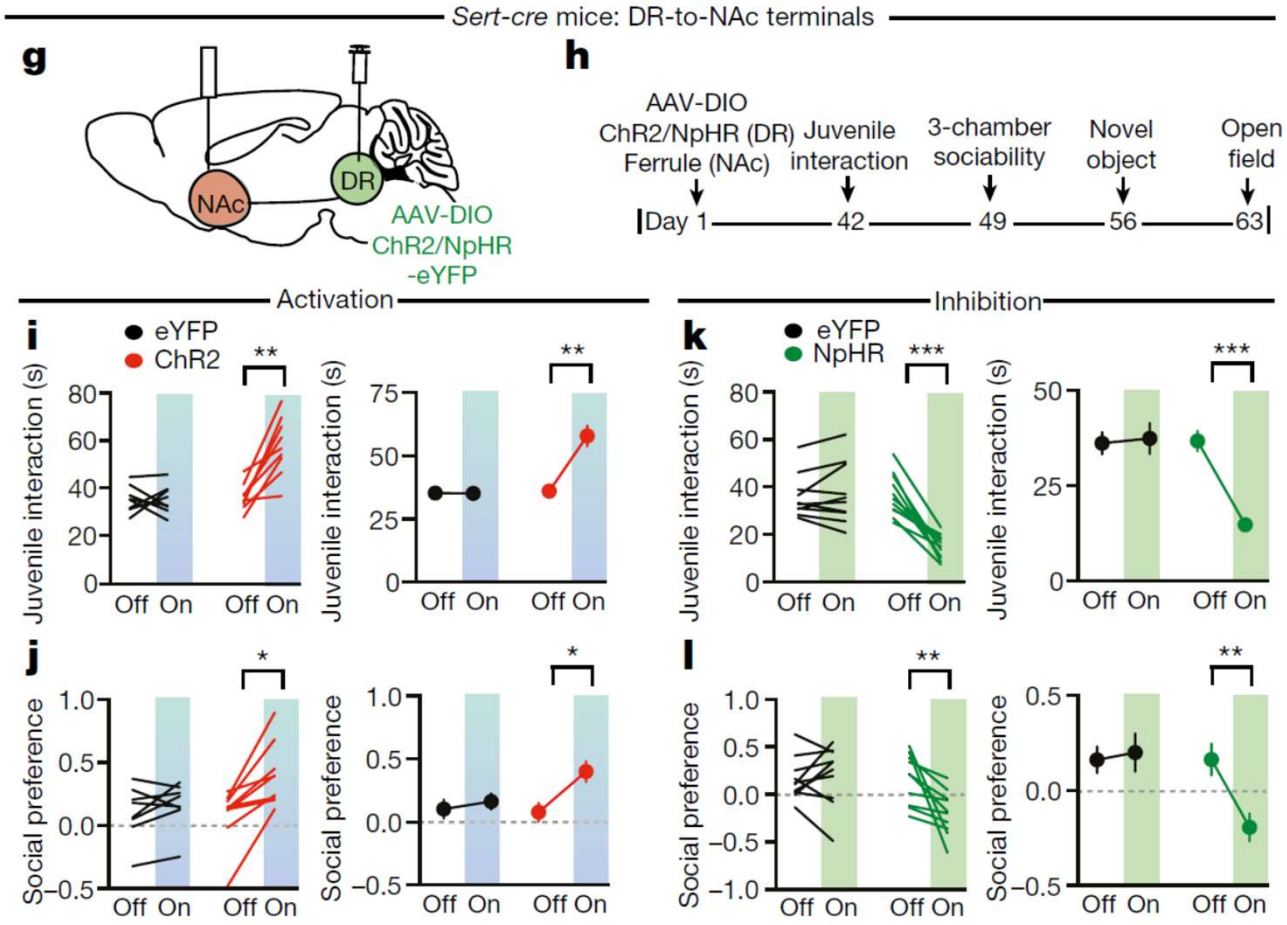


注射ChR2到中缝核，激动中缝核5-HT神经元活动，动物社交活动增加。

注射NpHR到中缝核，抑制中缝核5-HT神经元活动，动物社交活动减少。

Walsh et al, Nature 2018

中缝核-伏核5-HT神经通路对社交活动的双向调节



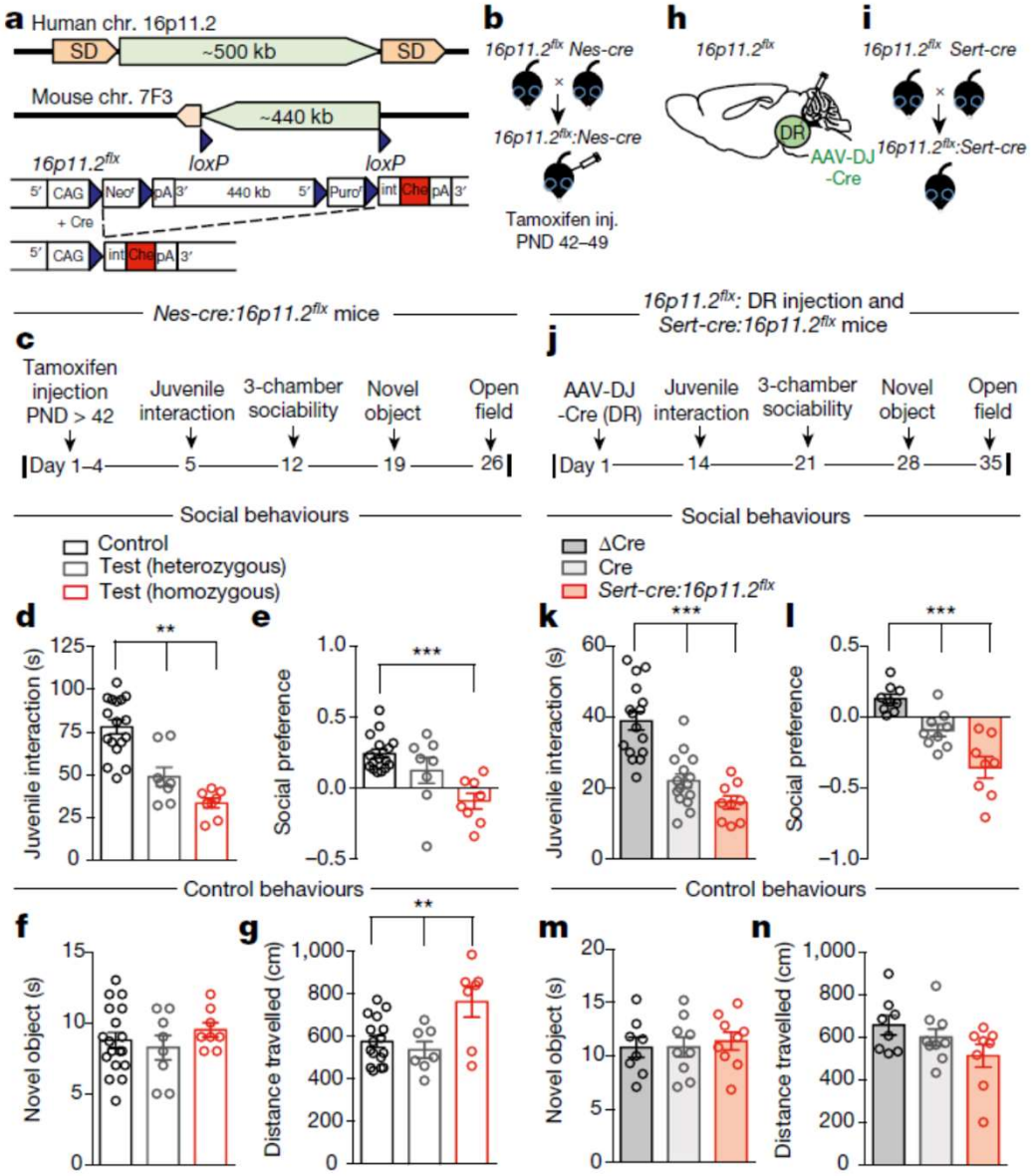
注射ChR2到中缝核，激动中缝核-伏核5-HT神经通路活动，动物社交活动增加。

注射NpHR到中缝核，抑制中缝核-伏核5-HT神经通路活动，动物社交活动减少。

进一步证实中缝核-伏核 5-HT通路在动物社交活动中起作用。

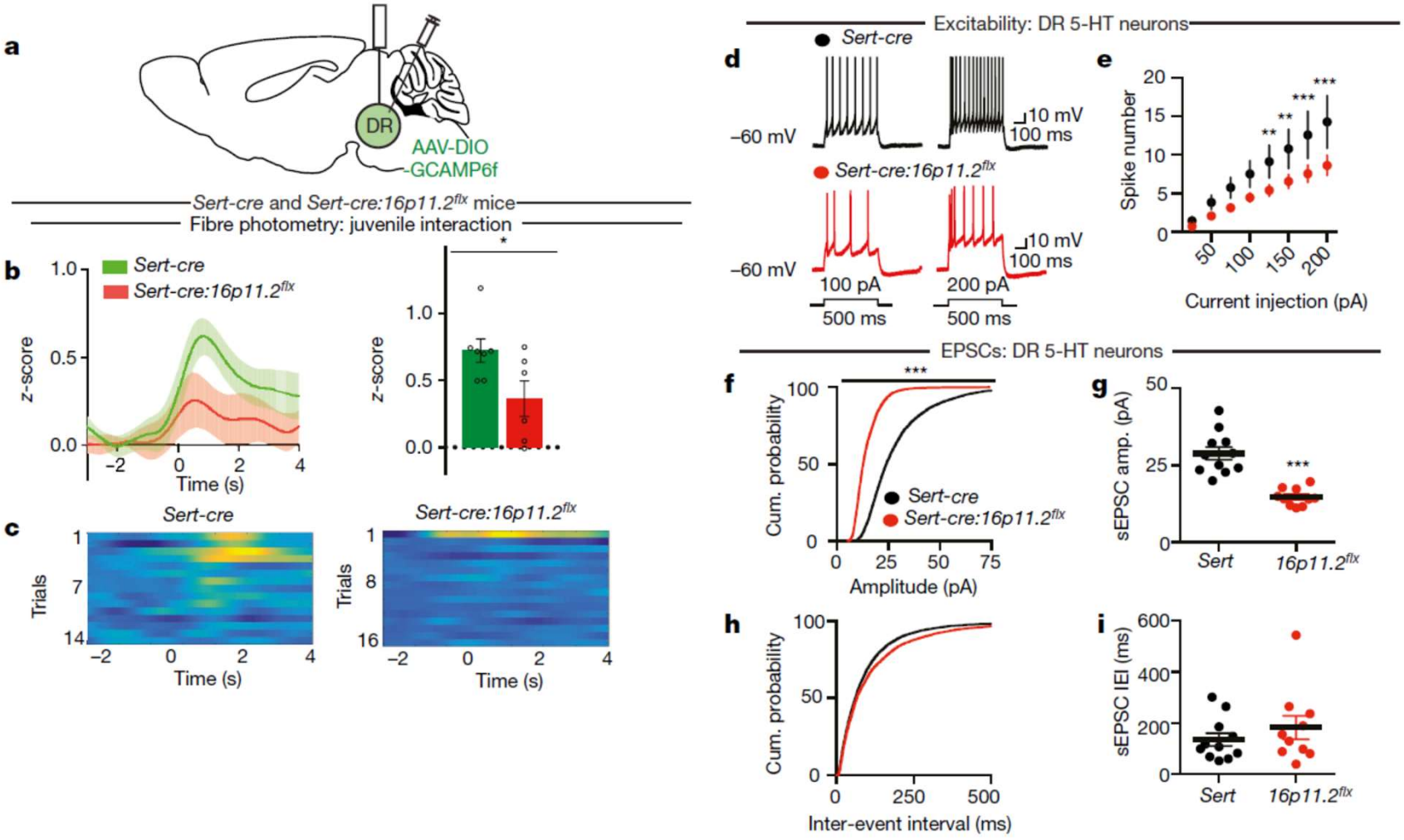
Walsh et al, Nature 2018

全脑或者**5-HT**神经元**16p11.2** 缺失减少动物社交活动



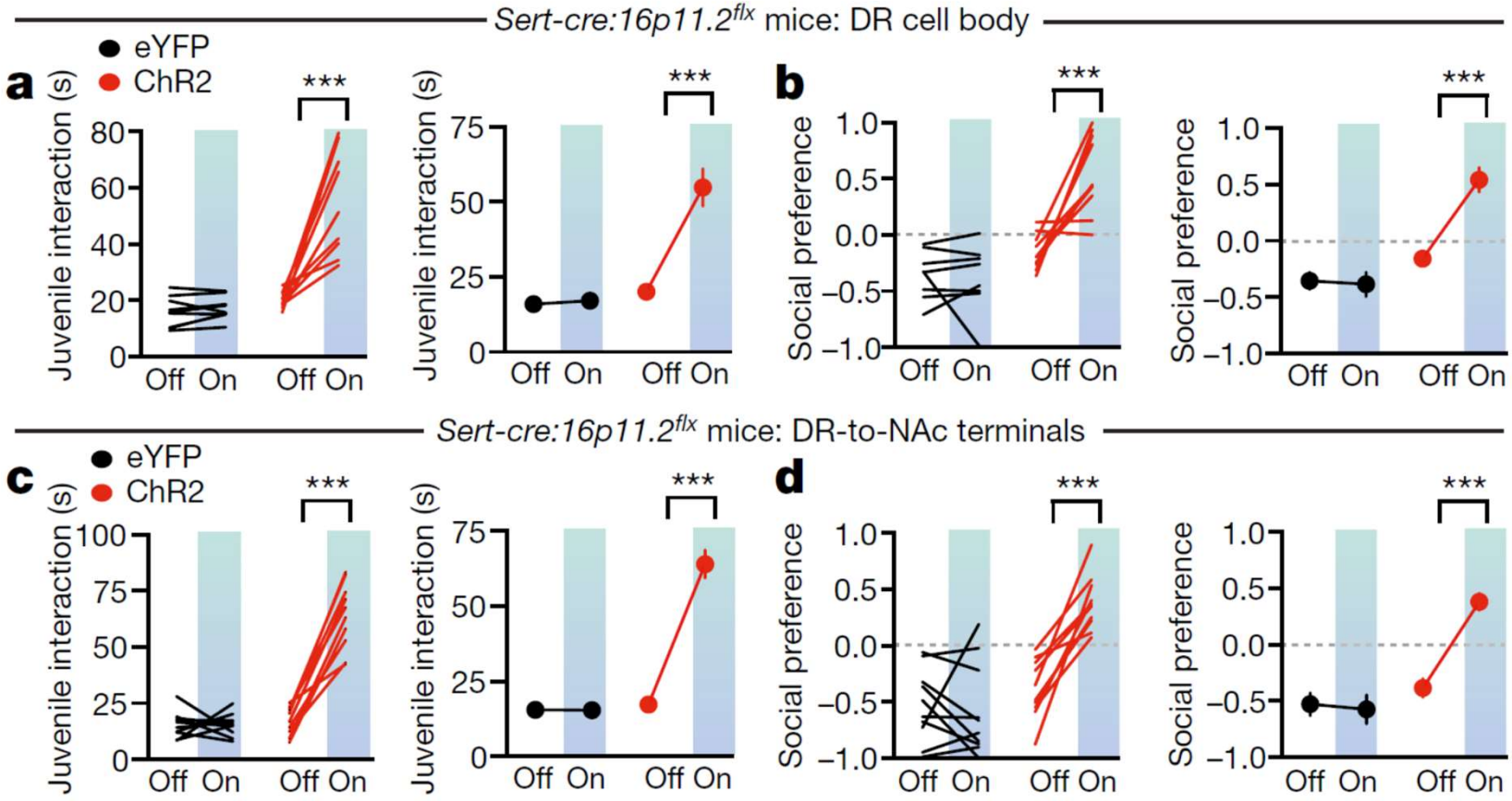
Walsh et al, Nature 2018

16p11.2 丢失造成中缝核5-HT神经元活动减弱、兴奋性下降和突触传递障碍



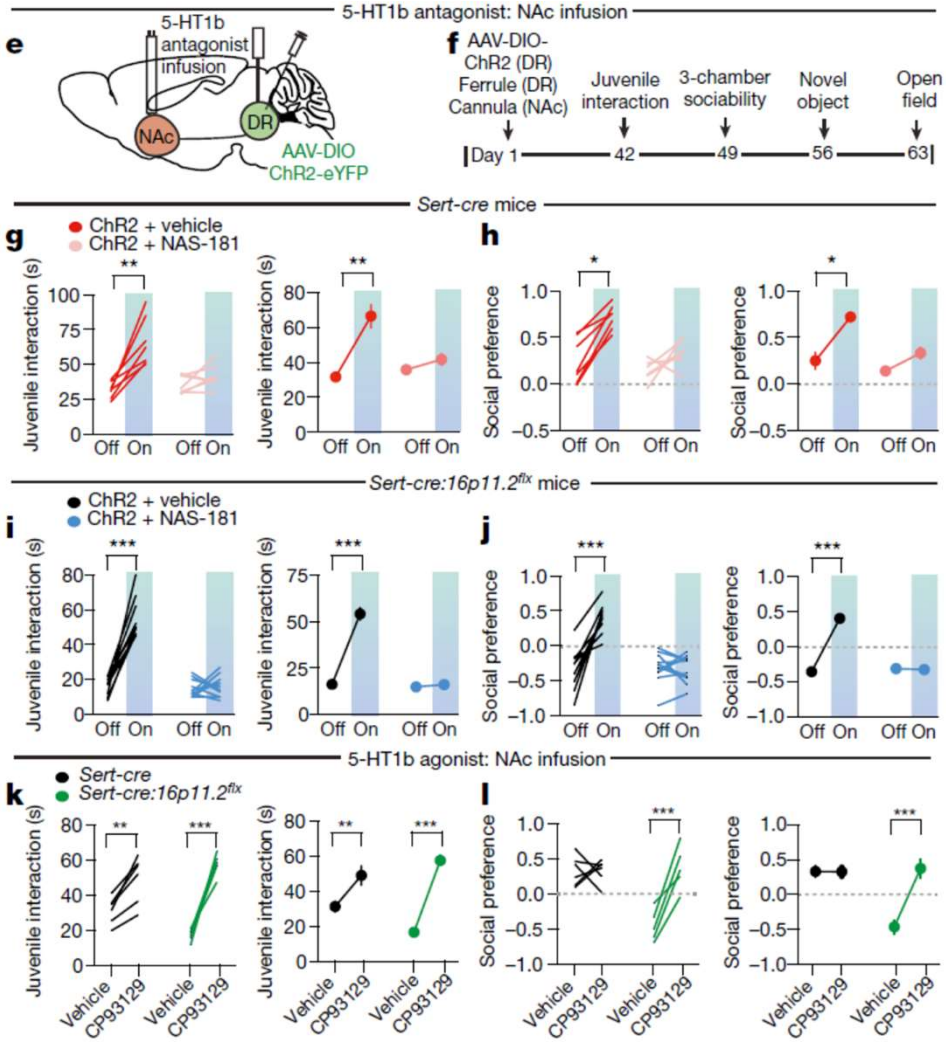
Walsh et al, Nature 2018

用光遗传学的办法，增加中缝核或者中缝核-伏核通路活动，能够改善16p11.2基因敲出鼠的社交障碍



Walsh et al, Nature 2018

伏核中微量注射5-HT1b受体阻断剂 NAS-181能够阻断刺激中缝核引起的社交行为改善，不仅在正常动物，也在基因敲出鼠上。

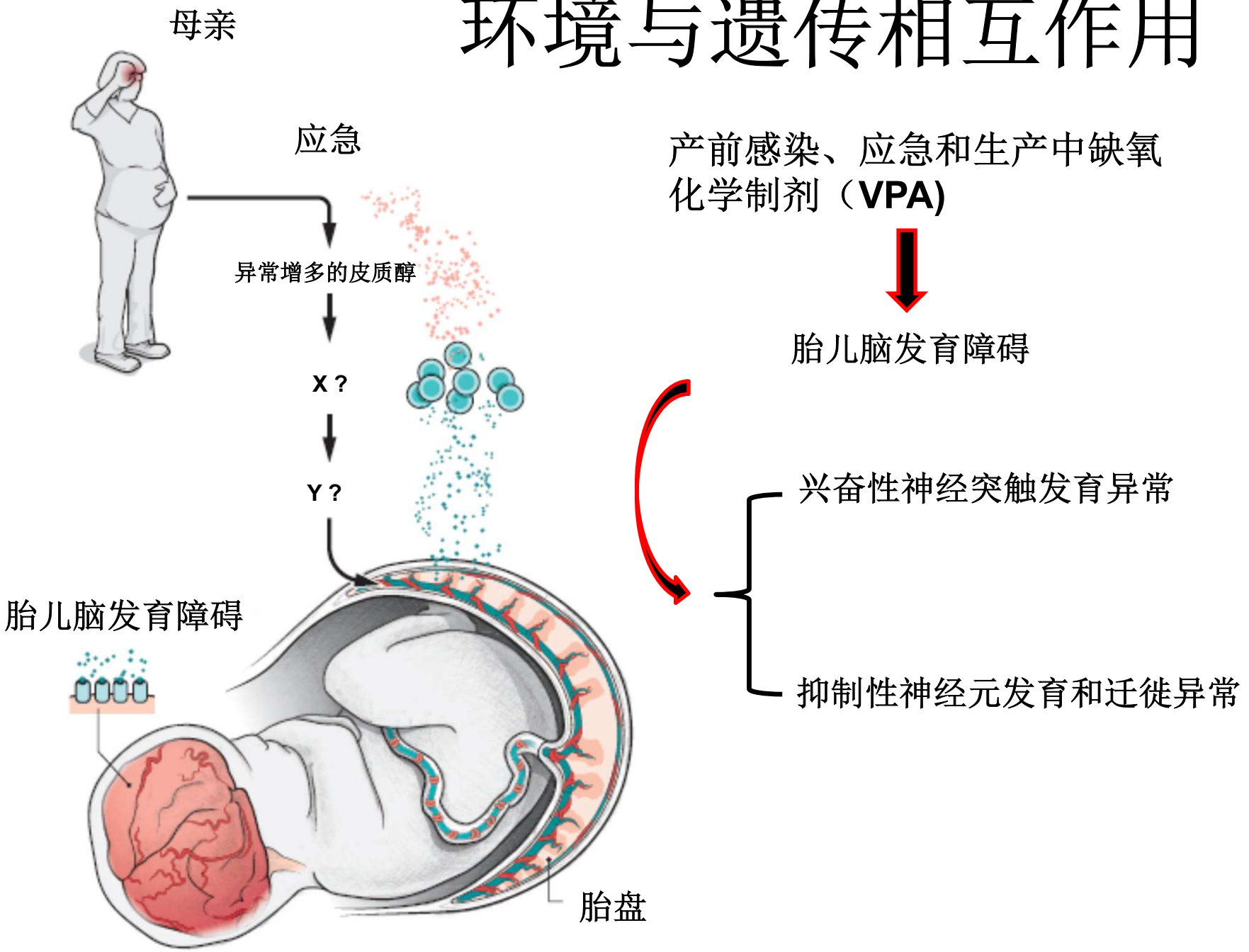


总之，增加5-HT在伏核释放，能够改善相对应16p11.2缺失的小鼠孤独症模型的行为缺失。

反过来，微量注射5-HT1b激动剂 CP93129能够增加正常动物社交活动并改善基因敲出鼠的社交障碍。

Walsh et al, Nature 2018

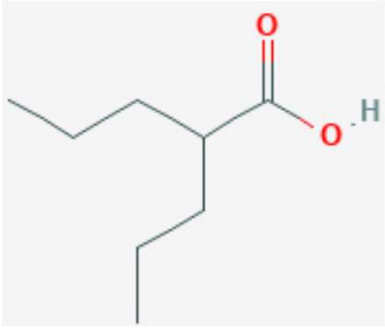
环境与遗传相互作用


母亲
应急
异常增多的皮质醇
X？
Y？
胎儿脑发育障碍
胎盘
产前感染、应急和生产中缺氧
化学制剂（VPA)
胎儿脑发育障碍
兴奋性神经突触发育异常
抑制性神经元发育和迁徙异常

frontiers in Behavioral Neuroscience

ORIGINAL RESEARCH
published: 21 August 2018
doi: 10.3389/fnbeh.2018.00182

Check for updates



丙戊酸钠

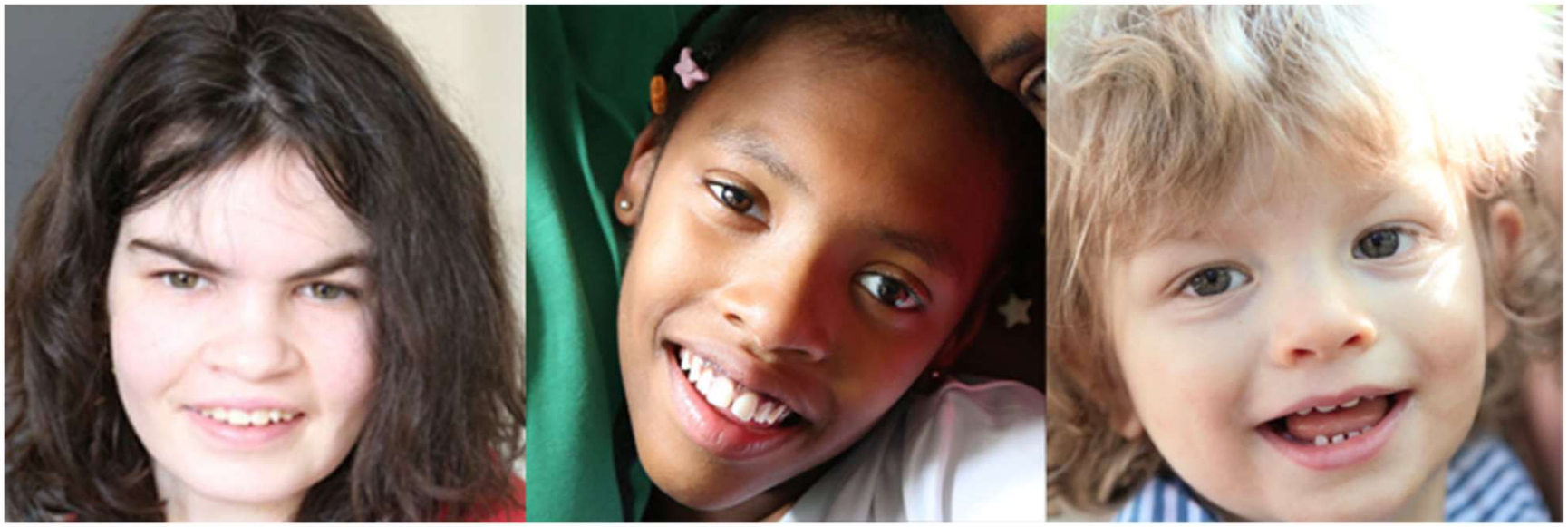
A Developmental Study of Abnormal Behaviors and Altered GABAergic Signaling in the VPA-Treated Rat Model of Autism

Qianling Hou[1,2], *Yan Wang*[1,2], *Yingbo Li*[1,2], *Di Chen*[1,2], *Feng Yang*[3]* and *Shali Wang*[1,2]*

[1]*Cerebrovascular Disease Laboratory, Institute of Neuroscience, Chongqing Medical University, Chongqing, China,* [2]*Department of Physiology, School of Basic Medical Sciences, Chongqing Medical University, Chongqing, China,* [3]*Lieber Institute for Brain Development, Johns Hopkins University Medical Center, Baltimore, MD, United States*

VPA造成老鼠的多个脑区突触兴奋/抑制失衡，包括PV表达下降和PV神经元数量下降，KCC2表达下降，造成脑内GABAergic 信号通路下降，引起老鼠自闭症样的行为障碍。

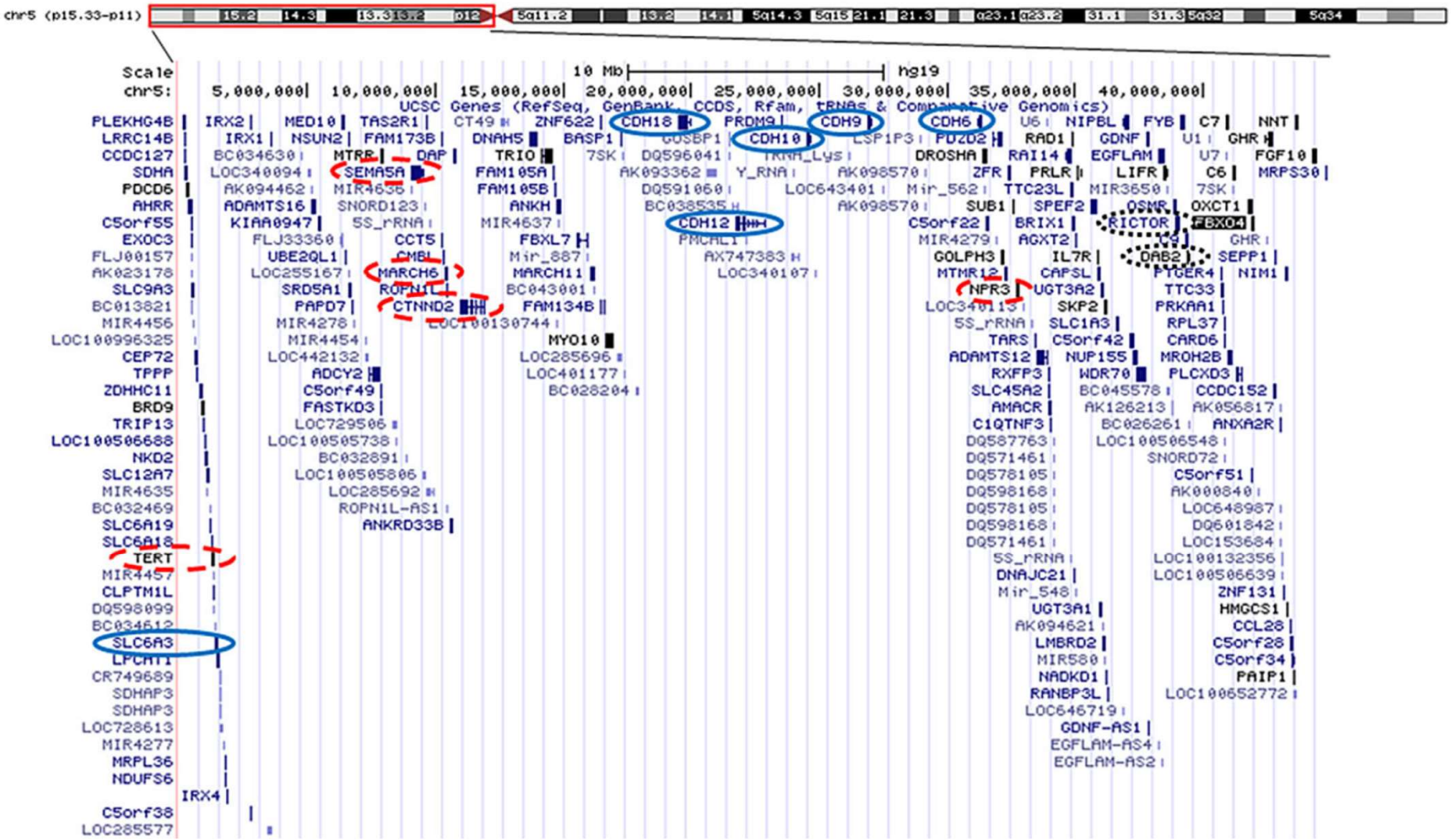
5p Deletions (Cri Du Chat Syndrome)
猫叫综合征



Left to right: Christina (21 years old), Brielle (9 years old), and Jack (22 months old) with 5p deletions.

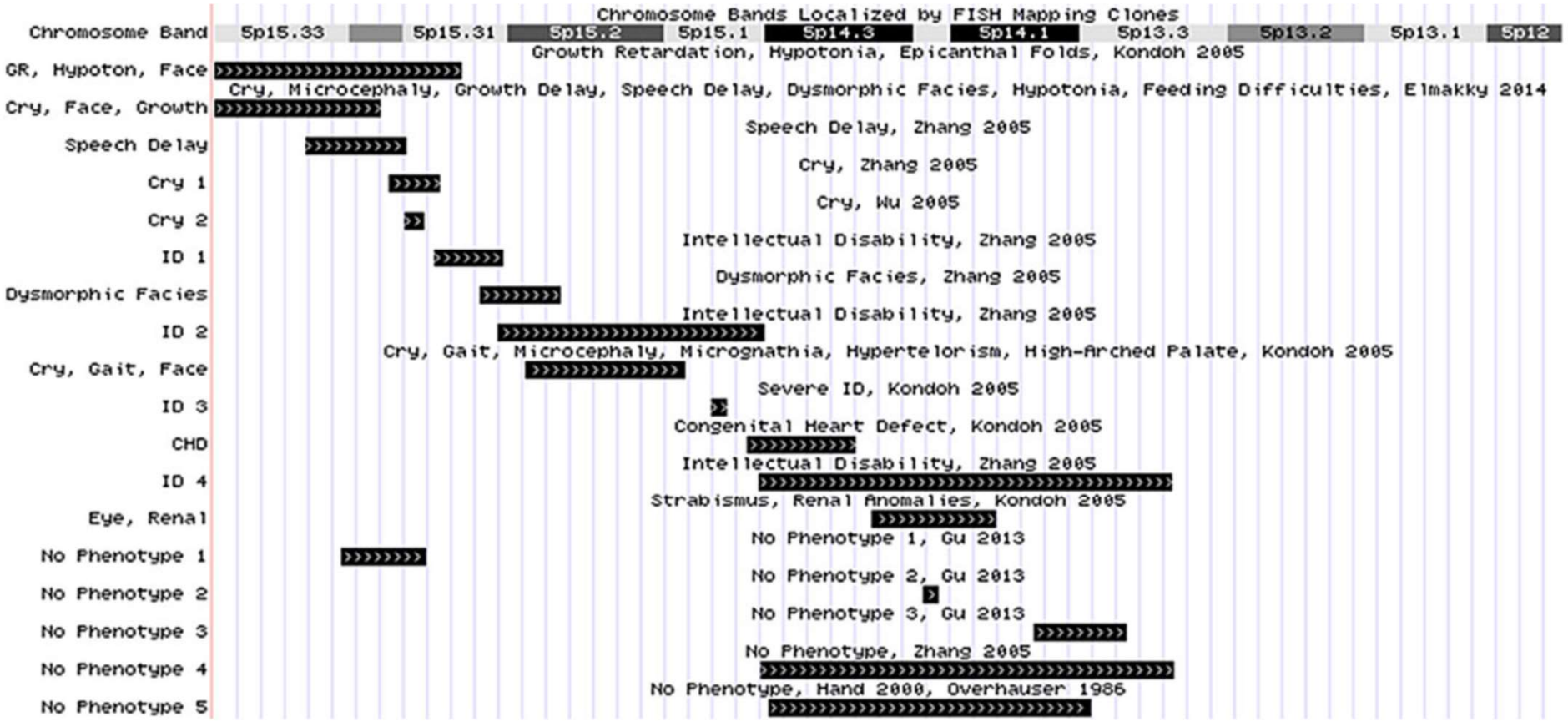
Nguyen et al, Am J Med Genet C Semin Med Genet 2015

5p Deletions



Nguyen et al, Am J Med Genet C Semin Med Genet 2015

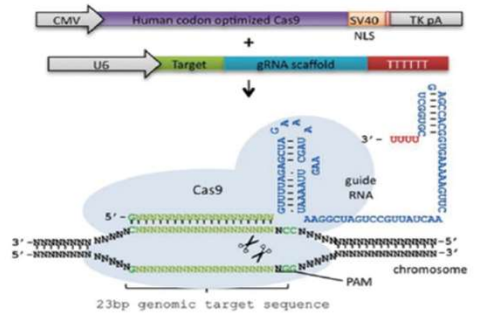
Chromosome 5p gene dosage map



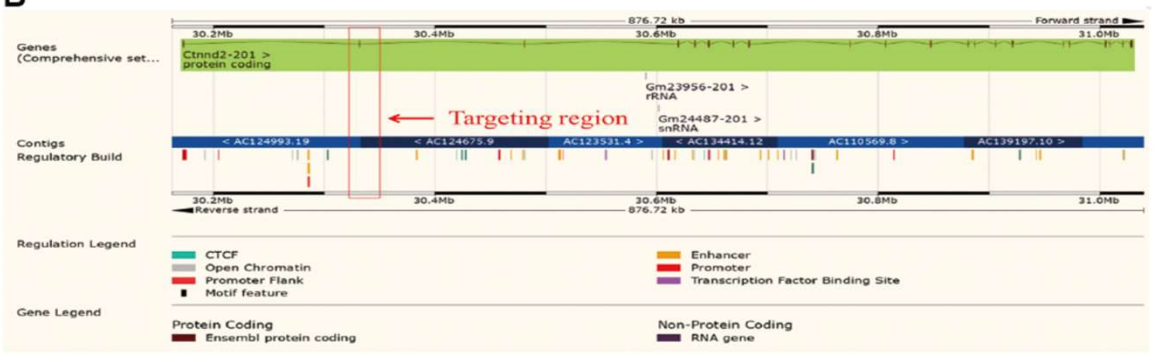
Nguyen et al, Am J Med Genet C Semin Med Genet 2015

Mutant CTNND2 mouse model associated with ASD

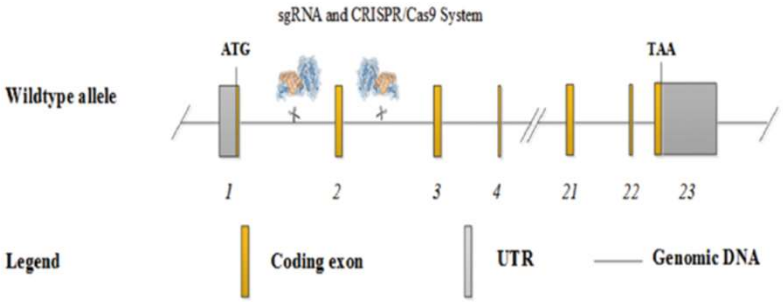
A



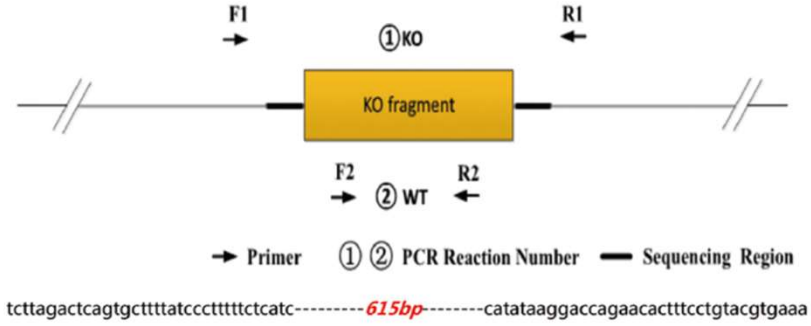
B



C



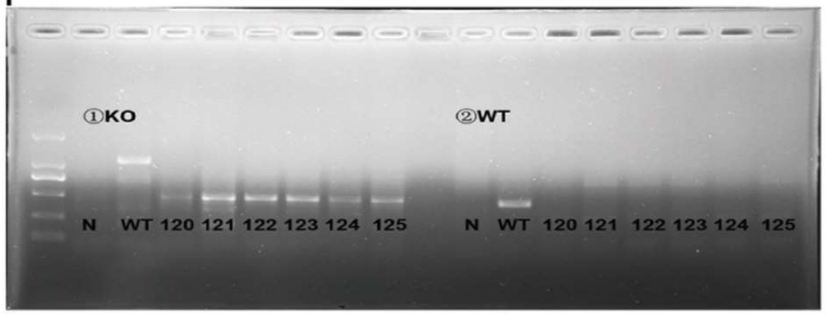
D



E

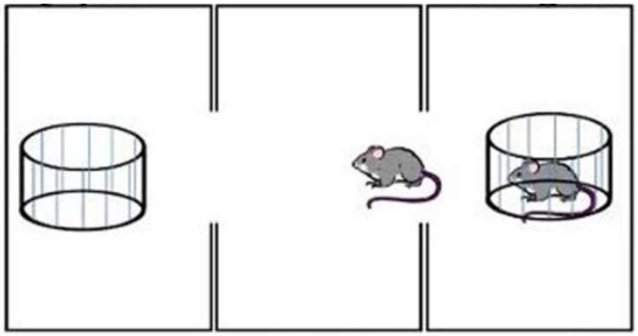
PCR reaction number	name of the primer	primer sequence	Product size
①KO	F1	TTCTGTATTTCACAGTACCAAC	WT:1074bp Targeted:~415bp
	R1	AACTCATCATAAGAAACACCTG	
②WT	F2	TGTTTGACTTCATTGTTACAG	WT:421bp Targeted:0bp
	R2	CAACTGTCACCCTACTTTAGT	

F

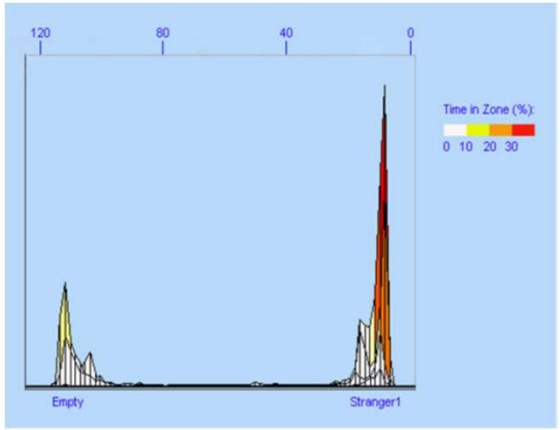


Unpublished data

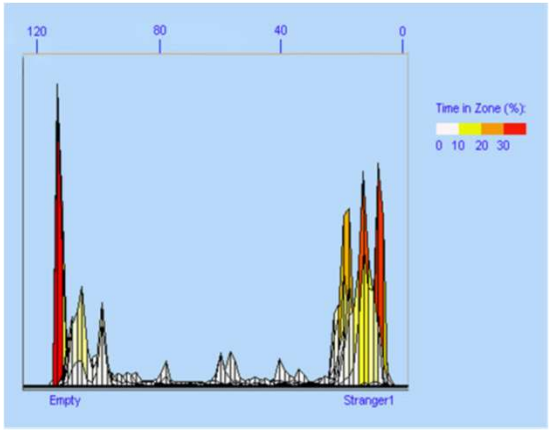
P compound修复CTNND2突变体导致的社交障碍



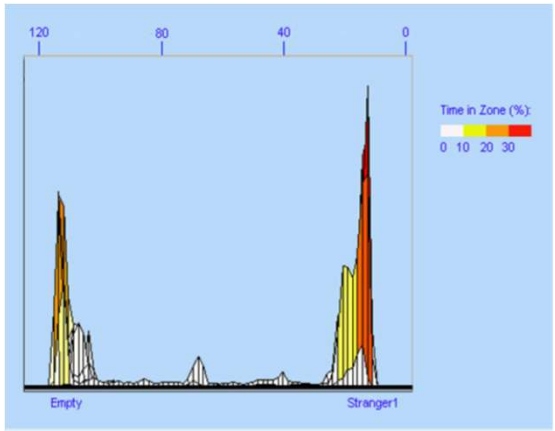
WT



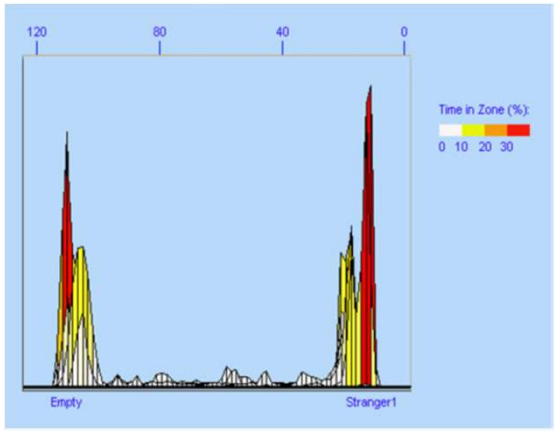
Mutant
CTNND2
+
P compound



Mutant
CTNND2

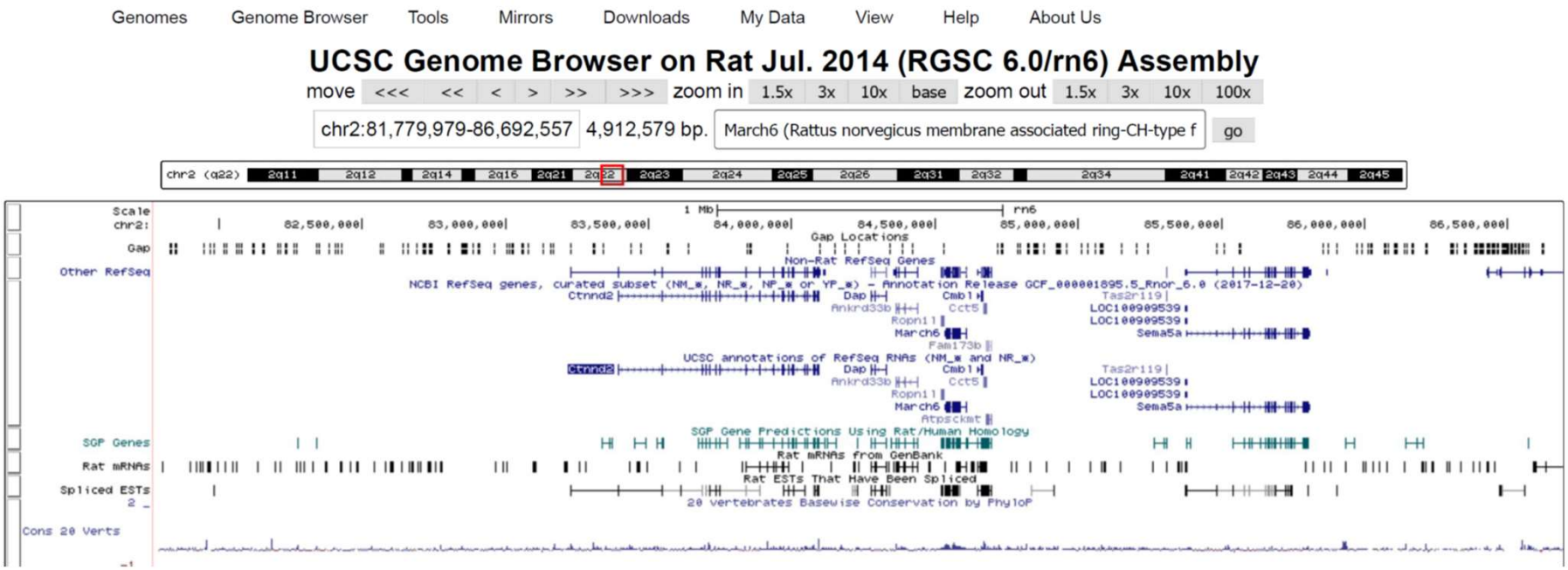


Mutant
CTNND2
+
G compound



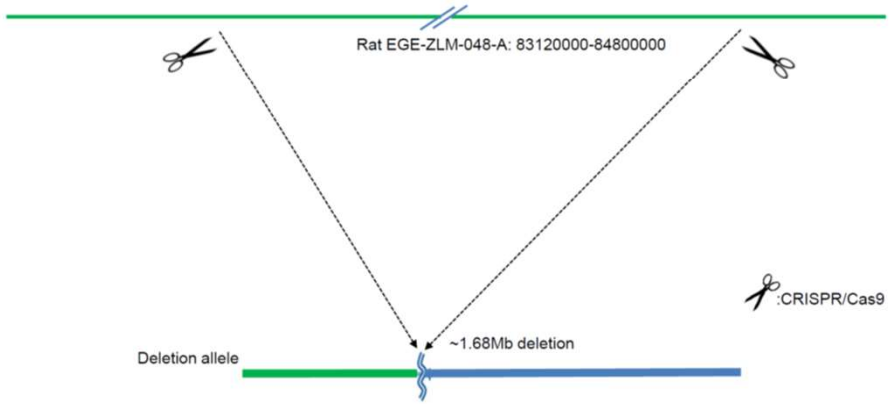
Unpublished data

5p deletion rat model



II. Targeting strategy-KO-EGE(CRISPR/Cas9) system

Wild type allele



Two sgRNAs will be designed to generate a ~1.68Mb chromosomal deletion including 83120000-8480000.

Unpublished data

孤独症药物精准治疗临床试验

Disorder	Study drug	ASD/neurocognitive outcomes
Tuberous sclerosis	Everolimus (RAD001)	ASD, memory, language skills, cognition, general executive function outcomes, behavioral changes, frequency or reduction of epileptiform events, reduced mTOR signaling
Rett syndrome	rhIGF-1	Behavior, cognition, cortical function, motor function
	Fingolimod (FTY720)	Slow regression of motor or language skills
	Dextromethorphan	Seizures, behavioral problems, cognition
	Glatiramer acetate	Epileptic activity, general behavior
	NNZ-2566	EEG, behavior, autonomic function
Fragile X syndrome	Acamprosate	Inattention or hyperactivity, social impairment, behavior, cognition
	NNZ-2566	Behavior, global and functional outcome measures
	Ganaxolone	Behavior, anxiety, attention, cognition
	Metadoxine (MG01CI)	Attention-deficit hyperactivity disorder
	Epigallocatechin-3-gallate (EGCG)	Improve intellectual disability, learning, memory, language
Angelman syndrome	Minocycline	Motor development, behavior, cognition, language
Down syndrome	RG1662	Cognition, behavior
	Low-dose nicotine	Cognitive improvement
	Donepezil (E2020)	Activities of daily living
	Thyroid hormone and folinic acid	Psychomotor development
Phelan-McDermid syndrome	rhIGF-1	Behavior, language, motor skills

PNAS

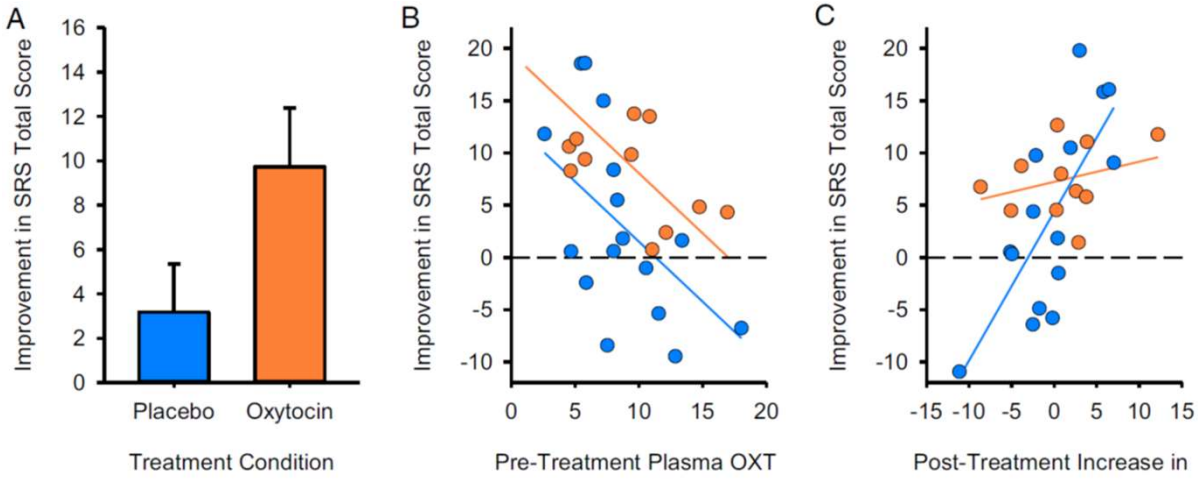
Intranasal oxytocin treatment for social deficits and biomarkers of response in children with autism

Karen J. Parker[a,1], Ozge Oztan[a], Robin A. Libove[a], Raena D. Sumiyoshi[a], Lisa P. Jackson[a], Debra S. Karhson[a], Jacqueline E. Summers[a], Kyle E. Hinman[a], Kara S. Motonaga[b], Jennifer M. Phillips[a], Dean S. Carson[a], Joseph P. Garner[a,c], and Antonio Y. Hardan[a]

[a]Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA 94305; [b]Department of Pediatrics, Stanford University, Stanford, CA 94305; and [c]Department of Comparative Medicine, Stanford University, Stanford, CA 94305

Edited by Michael L. Platt, University of Pennsylvania, Philadelphia, PA, and accepted by Editorial Board Member Michael S. Gazzaniga June 6, 2017 (received for review April 17, 2017)

test the efficacy and tolerability of 4-wk intranasal OXT treatment (24 International Units, twice daily) in 32 children with ASD, aged 6–12 y.



Vasopressin: A possible therapeutic for autism?

The Role of Vasopressin in the Social Deficits of Autism

Researchers at the Stanford University School of Medicine are seeking participants for a study examining the effectiveness of vasopressin, a neuropeptide, in treating children with autism spectrum disorder. Difficulty with social interactions is characteristic of people with autism, who often have problems interpreting facial expressions or maintaining eye contact while talking with someone. There are currently no effective medicines available to treat social problems in individuals with autism. Neuropeptides, such as vasopressin and oxytocin, are molecules used by neurons in the brain to communicate with one another. Vasopressin is closely related to oxytocin, which is currently being tested as a treatment for autism, and has been shown to enhance social functioning in animals. Animal studies have shown that when the proper functioning of vasopressin is experimentally altered, animals develop a variety of social deficits, including impaired memory for peers and a reduced interest in social interaction. Researchers found that when vasopressin was administered to mice with a genetically induced form of autism, their social functioning improved. Vasopressin is already approved by the Food and Drug Administration for use in humans, and has proved to be a successful treatment for some common pediatric conditions, including bedwetting. Similar to oxytocin, it also has been shown to improve social cognition and memory in people who do not have autism. The researchers will test the effects of vasopressin on social impairments in 50 boys and girls with autism, ages 6 to 12 years old. The study will last four weeks for each participant. Participants will receive either vasopressin or a placebo nasal spray. At the end of this phase of the study, those who received the placebo will have the option of participating in a four-week trial during which they will be given vasopressin. Stanford is the only site for the study. Participants do not need to live locally but will need to come to the Stanford University Department of Psychiatry and Behavioral Sciences for study visits.

Stanford is currently not accepting patients for this trial.

Lead Sponsor:
Stanford University
Collaborator: National Institute of Mental Health (NIMH)

Stanford Investigator(s):
Karen J. Parker, PhD
Dr. Kyle Hinman
Antonio Hardan, M.D.

Intervention(s):
Drug: Vasopressin
Drug: Placebo

Phase:
Phase 2

怎样帮助孤独症患儿

1. 到专科医院，找有经验的儿科医生。

2. 到孤独症康复中心，进行儿童语言和行为训练。

孤独症的康复训练

对于孤独症患儿来讲，只有早发现、早干预、进行行为矫治，才能帮他们缩小与正常社会的差距，让他们早日融入社会。

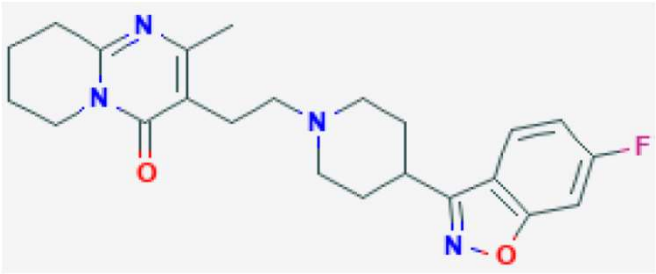
孤独症没有特效药物治疗。

早期诊断早期干预可以改善孤独症的预后，因此孤独症治疗一般认为是年龄越小、效果越好。

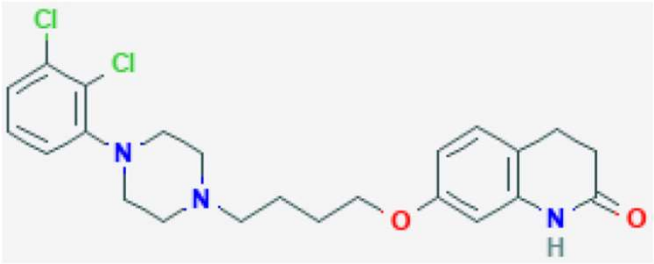
1. 早发现，早治疗。治疗年龄越早，改善程度越明显。
2. 促进家庭参与，让父母也成为治疗的合作者或参与者。
3. 坚持以非药物治疗为主，药物治疗为辅。
4. 治疗方案应个体化、结构化和系统化。
5. 治疗、训练的同时要注意患儿的躯体健康，预防其他疾病。
6. 坚持训练，持之以恒。

孤独症辅助药物治疗

1. 利培酮 (risperidone) FDA批准，2006



2.阿立哌唑(aripiprazole) FDA批准, 2007



治疗自闭症患儿伴随的烦躁不安

由于有上百个基因突变与孤独症有关，不同患者可能是由不同的基因突变引起的，看来解决因为遗传基因突变引起的孤独症，可能最终解决的办法还得靠Gene therapy。

孤独症患儿能够上学吗？

当然可以！

天生我才必有用！

很多孤独症患者拥有特殊技能：视觉能力、音乐、数学、艺术和科学。

Thomas Sudhof
(1955-present)

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