

Model	Principle Paper	Related Papers	Iteration of Conditional Model
Constitutive Haploinsufficient Mouse Models of SCN2A			
<i>Scn2a +/-</i>	Planells-Cases et al., 2000	Planells-Cases et al., 2000	
		Mishra et al., 2017	
		Middleton et al., 2018	
		Ogiwara et al., 2018	
		Lena and Mantegazza 2019	
		Spratt et al., 2019	
		Tatsukawa et al., 2019	
		Miyamoto et al., 2019	
		Spratt et al., 2021	
		Indumathy et al., 2021	
		Tamura et al., 2022	
		Schamiloglu et al., 2023	
Wang et al., 2024			
Marcantonio et al., 2023			
<i>Scn2a+/-; Kcna1-/-</i>	Mishra et al., 2017	Mishra et al., 2008 Indumathy et al., 2021	
<i>Scn2a+/-; Kcna1+/-</i>		Indumathy et al., 2021	
<i>Nav1.2 adult</i>		Gazina et al., 2015	
<i>Scn2a fl/+</i>		Shin et al., 2019	
<i>Scn2a +/KI</i>	Tamura et al., 2022	Tamura et al., 2022	
Premature Stop Codon Models			
<i>Scn2a R102X/+</i>		Ogiwara et al., 2018	
Conditional Mouse Models of Scn2a Haploinsufficiency			
<i>Ei14::Scn2a +/-</i>	Spratt et al., 2019	Spratt et al., 2019	PV-Cre SOM-Cre
<i>Scn2a +/fl</i>		Spratt et al., 2021	CaMKII α -Cre EF1 α -Cre (Scn2a +/fl and Scn2a fl/fl)
		Wang et al., 2024	Alpha6-Cre
<i>SCN2A ff</i>		Gould and Kim 2021	PDGFRA - Cre Actin- Cre
<i>Scn2a fl/+</i>	Ogiwara et al., 2018	Yamagata et al., 2017	
		Ogiwara et al., 2018	Vgat-Venus Emx1-Cre Vgat-Cre Vgat-Venus
		Tatsukawa et al., 2019	Emx1-Cre Vgat-Cre
		Miyamoto et al., 2019	Emx1-Cre Vgat-Cre
		Miyamoto et al., 2019	Trpc-Cre Ntsr-Cre
<i>Scn2a fl/fl</i>		Suzuki et al., 2023	mPFC-Cre VTA-Cre
<i>Scn2a +/KI</i>		Tamura et al., 2022	EF1 α -Cre
<i>Scn2a fl/fl</i>		Ma et al., 2022	SCN-Cre
Additional Mouse Models of Scn2a Reduction			
<i>Scn2a :OB GC - shRNA</i>		Nunes and Kuner, 2018	
<i>Scn2aΔ1898/+</i>		Wang et al., 2021	
<i>Scn2a gtKO/gtKO</i>	Eaton et al., 2021	Eaton et al., 2021	
		Ma et al., 2022	
		Wu et al., 2024	
<i>Scn2a ASO</i>		Li et al., 2023	
SCN2A Gain of Function Mouse Models			
<i>Scn2a Q54</i>	Kearney et al., 2001	Kearney et al., 2001	
		MacDonald et al., 2004	
		Bergren et al., 2005	
		Bergren et al., 2009	
		Kile et al., 2008	
		Anderson et al., 2014	
		Kim et al., 2016	
		Calhoun et al., 2016	
		Hawkins & Kearney, 2016	
Thompson et al., 2017			
<i>Scn2a A263v /+</i>		Schattling et al., 2019	
<i>Scn2a Q/+</i>		Li et al., 2021	
Other SCN2A Mouse Models			
<i>Scn2a E/+</i>	Echeveria-Cooper et al., 2022	Echeveria-Cooper et al., 2022	
		Echeveria-Cooper et al., 2023	
		Echeveria-Cooper and Kearney, 2023	

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Planelis-Cases Scn2a +/- Mouse Model														
Mishra et al., 2017	Scn2a +/- (Planelis-Cases model)		2 - 3 months							-ND in seizure threshold or epileptiform activity -ND in cardiac activity with EEG-ECG recordings -ND in latency to GTC seizures	-ND in brain-heart association	RED = Decrease BLUE = Increase/Altered ND = No Difference		
Middleton et al., 2018 (males only)			4 - 6 months		-Delayed learning in spatial working memory task -Slower learning in Barnes maze							-Decrease in the peak firing rate of piriform cortex during SPW-R events -Lower strength of assembly during SPW-Rs -Truncated hippocampal replay sequences	OFT = Open Field Test EPM = Elevated Plus Maze FST = Forced Swim Test TST = Tail Suspension Test USV = Ultrasonic Vocalization PPI = Prepulse Inhibition mPFC = Medial Prefrontal Cortex ECoG = Electroencephalogram PTZ = Pentyleneetetrazol FSI = fast-spiking interneurons EPSCs = excitatory postsynaptic currents VOR = Vestibular Ocular Reflex	
Ogiwara et al., 2018			6 - 11 weeks								-ND in susceptibility to kainic acid induced seizures -Frequently abnormal ECoG recordings with absence-like discharges with SWDs -Higher maximum amplitude and spike numbers during a seizure episode -Shorter latency to have absence seizure-like immobility when injected with PTZ		-Higher prevalence and incidence of epileptiform discharges in mPFC -Impaired excitatory neural activity	
Lena and Mantegazza, 2019 (males only)			Juvenile: P22 - P44	-Decreased amount and length of USVs produced -Decreased social interaction in the first two minutes of reciprocal social interaction test	-Slight decrease of spontaneous alternations in Y maze -Decreased preference for novel object in NOR task	-Increased acquired motor learning on rotarod	Increased grooming -Increased marble burying	-Reduced anxiety in EPM -Reduced anxiety in OFT -ND in locomotion in OFT	-ND in odor discrimination task				-Decreased immobility in TST	
			Adult: P60 - P95	-Decreased amount and length of USVs produced -ND in reciprocal social interaction test	-ND in number of visits or spontaneous alternations in Y maze -ND in preference for novel object in NOR task -Slightly slower acquisition latency in Barnes maze test	-ND in motor learning in rotarod	-ND in grooming -ND in marble burying	-ND in anxiety in EPM -ND in anxiety in OFT -ND in locomotion in OFT	-ND in odor discrimination task				-Slight decrease in immobility in minutes four to six of TST	
Spratt et al., 2019			Age not reported	-Females showed no preference for novel stimuli in two-chamber social task	-Males had slightly impaired reversal learning water T-maze -ND in spontaneous alternation assay	-ND in rotarod -ND in balance beam	-ND in grooming -ND in nesting assay	-Females had reduced anxiety in EPM -ND in OFT						
Tatsuwaka et al., 2019 (males only)			P6 for USV +8 - 31 weeks for other assays	-Increased sociability in e-chamber assay -Slight dominant behavior in tube test -Deficit in social approach toward stranger mice in resident-intruder test -ND in social communication in USV	-Enhanced fear conditioning retention -Impaired extinction of fear-related memory	-Deficient motor coordination in rotarod	-Increased rearing in OFT	-Reduced anxiety in EPM -Reduced anxiety in OFT -Increased anxiety in light/dark assay					-Higher immobility in FST -Immobility in TST -ND in PPI -Increased activity in the gamma band in the mPFC	
Miyamoto et al., 2019			> 8 weeks									-Have SWDs during behavioral quiescence	-Slight decrease in EPSCs in FSIs	
Indumathy et al., 2021			28 - 34 days	-ND in sociability in three-chamber assay -Decreased preference for novel stranger mice in social novelty assay		-Reduced marble burying -Increased grooming							-ND in nestlet shredding	
Schamiloglu et al., 2023			P54 - P119			-ND in learning the standard dynamic foraging task or variations of the assay where mice are head-fixed, the block length varies, there is reward optimization, or the cues vary -Slight increase in frequency to pick higher reward side in foraging assay -Males had inflexible choice behavior during mid-block performance in the unpredictable paradigm of the dynamic foraging assay -ND in intertrial interval in dynamic foraging assay							-Spontaneous behavioral seizures in four of twenty five mice at the end of a day's training and one of the four mice died	
Wang et al., 2024			P60 - P90										-Consistently elevated VOR gain in different rotation frequencies -Decreased Purkinje cell firing rate	
			Juvenile: P21 - P44	-Higher sociability in e-chamber assay -ND in social novelty in three-chamber assay	-ND in preference for displaced object in novel object recognition task -Lower entries into the of the Y maze -Increased decision-making latency in Y maze	-Higher latency to fall on day one of rotarod	-ND in grooming -ND in marble burying	-ND in EPM locomotion -Reduced anxiety in EPM -ND in anxiety in OFT -ND in OFT locomotion	-ND in odor discrimination task				-ND in latency of reaction to stimuli in hotplate assay -ND in latency before withdrawal in coldplate assay	

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Marcantonio et al., 2023 (females only)			Adult: >P60	-Higher sociability in three-chamber assay -Altered interaction with novel mouse in three-chamber assay	-ND in preference for left in NOR task -Lower entries into the three arms of Y maze - Increased decision-making latency in Y maze -Reduced percent of spontaneous alternations in Y maze	-ND in latency to fall in rotarod	-ND in grooming ND in marble burying	-ND in EPM locomotion - ced anxiety in EPM -ND in anxiety in OFT ND in OFT locomotion	-ND in odor discrimination task		-ND in latency of reaction to stimuli in coldplate assay -Decreased latency before withdrawal in coldplate
Other Constitutive Haploinsufficient Mouse Models Behavior											
Mishra et al., 2017	<i>Scn2a^{+/-};</i> <i>Kcna1^{-/-}</i>		2-3 months							<i>Scn2a^{+/-}</i> decreases spontaneous seizure duration in <i>Kcna1^{-/-}</i> mice	Nav1.2 reduction does not ameliorate cardiac phenotypes in <i>Kcna1^{-/-}</i> mice.
Indumathy et al., 2021	<i>Scn2a^{+/-};</i> <i>Kcna1^{+/-}</i>		28-34 days	-ND in sociability - Reduced social novelty sniffing ND in sociability or social novelty			-Reduced nestlet shredding and marble burying -ND in grooming and nestlet shredding -Reduced marble burying				
Gazina et al., 2015 (males only)	<i>Nav1.2 adult</i>		53 days >=	-ND in social interaction -16x more likely to jump out of social interaction box	ND in memory and spatial learning on Y-maze and Morris water maze	ND on rotarod, locomotion or in grip strength		-ND in OFT or Light-Dark box Reduced anxiety in EPM		Spontaneous seizures - More susceptible to PTZ-induced seizures	ND in thermal pain response, acoustic startle, PPI, or weight
Shin et al., 2019 (males only)	<i>Scn2a fl+</i>		2-4 months 4 days - 3 weeks	-ND social approach and communication - Increased direct social interaction -ND in number and duration of USVs -Slight increase direct social interaction	-Reduced Spatial learning and memory on Morris water maze -Increased Fear memory	ND on Rotarod -ND in locomotion in novel environments - Decreased locomotion in familiar environments	ND in grooming and rearing behaviors	-ND in anxiety for OFT, EPM and Light-Dark box Mild light induced hypoactivity		Spontaneous seizures -ND in susceptibility to PTZ-induced seizures	ND for novel object recognition ND in mother attachment behaviors
Hypomorphic Scn2a Mouse Model Behavior											
Wang et al., 2021	<i>Scn2a Δ1898/+</i>		>= 30 to 44 days	-Males displayed increased social interaction with novel mouse in 3-chamber - After repeat exposure to the same mouse, males, still displayed increased social interaction		ND in general locomotion	ND in time spent grooming	ND in OFT - Reduced anxiety-like behaviors on EPM			
Eaton et al., 2021	<i>Scn2a gKO;gKO (AKA Scn2a Trap)</i>		3 to 5 months		-Decreased novel object exploration in novel object -Decreased number of entries to, duration in, and preference for the novel arm of Y-maze	-ND activity, tail posture, limb grasping, extension, shivering reflex -Decreased grip ability in SHIPRA -Females traveled longer -Decrease in distance traveled in OFT -Performed with increased brightness	-Decreased overall nest building -Decreased quality of nests built -Increased grooming -Increased marble burying -Slightly increased induced digging	-Increased anxiety-like behavior in low and bright light OFT -ND freezing behavior in low light OFT -Increased freezing in OFT performed with high intensity luminescence	-ND overall odor discrimination Increased in time for discrimination		Increased water and food intake -Increased frequency of fecal boli in males -Lower body position rating, less trunk curl and postural reflex when held by SHIPRA -Decreased tolerance for heat and cold temperatures on thermal/cold plate assay -ND for dynamic hot plate Increased startle response -Decreased startle response in PPI
Ma et al., 2022			> 6 weeks			Impairment of wheel-running activity in light-dark conditions					Abnormal sleep patterns
Wu et al., 2024			3 to 4 months		Impaired learning and memory on Morris water maze and Y-maze						
Conditional and other Mouse Models of Scn2a Insufficiency											
Wang et al., 2024	<i>Scn2a fl/fl</i>	Alpha6-Cre	60 to 90 days								Altered VOR
Tatsukawa et al., 2019	<i>Scn2a fl/+</i>	Emx1-Cre	8 to 9 weeks (Male Only)			Increased rearing in OFT		-Increased time in center of OFT -Trend of entering open arms of EPM more			
		Vgat-Cre			ND in locomotion or rearing		-ND OFT Reduced anxiety-like behaviors on EPM				
Miyamoto et al., 2019	<i>Scn2a fl/fl</i>	Emx1-Cre	>= 8 weeks							-SWDs present during behavioral quiescence -Inactivation of the CPU or thalamus by muscimol injection suppresses SWDs	
		Vgat-Cre								No spontaneous SWDs	
		Trpc-Cre								Spontaneous SWDs	
Ma et al., 2022	<i>Scn2a fl/fl</i>	Ntsr-Cre	3-5 months							No spontaneous SWDs	Sleep Disturbances
Suzuki et al., 2023	<i>Scn2a fl/fl</i>	mPFC-Cre	18 to 19 weeks	Increased sociability in three chamber social approach		-Less distance traveled in three chamber social assay -Less distance travelled and fewer rearing events in OFT		Increased anxiety in OFT			Reduced PPI
		VTA-Cre	11- 13 weeks	ND sociability in 3 chamber social approach		Reduced rearing in OFT		ND OFT			Increased percentage of PPI of startle response to 120 dB sound with 74 or 78 dB prepulse
Nunes and Kuner, 2018	<i>Scn2a -OB GC-shRNA</i>		49 to 63 days						Reduced speed in odor discrimination		

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Li et al., 2023	Scn2a ASO		2-3 months	-Impaired social approach - Increased social avoidance in 3-chamber assay		Increased locomotion in OFT	Impaired nest building behavior	-Decreased anxiety and ability to assess risk in EPM - Increased anxiety-like behaviors in OFT		-No spontaneous seizures or detectable ictal features - Augmented seizure response to PTZ treatment	