Mouse Model	Deficient Phenotype	Preserved Phenotype	Authors
BACTgDyrk1a	Increased brain weight (9W) MWM Acquisition and probe (2M) Increased LTP Decreased LTD	Body weight (9W), Cued MWM, Rotarod training	(Ahn et al., 2006)
	Increased spine density of pyramidal PFC neurons (4-5M), Increased PSD95 protein levels in pyramidal PFC neurons (4-5M), Decreased LTP, Increased LTD	Spine length of pyramidal PFC Neurons (4-5M)	(Thomazeau et al., 2014)
	Rotarod (higher speeds), Accelerating Rod Spontaneous Alternation in Y-maze MWM latency, thigmotaxis, MWM probe	SHIRPA protocol, open field activity, rotarod at lower speeds, accelerating rod, cued MWM	(Souchet et al., 2014)
	Decreased body weight & length (P30) Increased brain weight (weaning to adulthood)	Body weight (P15, P60) Body length (P60) Brain weight (P0) Cerebellum size	(Guedj et al., 2012)
YACTgDyrk1a	MWM acquisition, reverse platform Locomotor hypoactivity	LTP PPI	(Smith et al., 1997)
	Passive avoidance acquisition (P15) Locomotor hyperactivity Increased brain weight (P21, adult) Increased neuron cell size in the hippocampus and cortex (adult) Increased sized of hypothalamus and septum	Locomotor activity thigmotaxis, rearing, grooming, jumping, sniffing Brain weight (P3) Body weight	(Branchi et al., 2004)
	Increased brain weight and volume (3M) Increased thalamus-hypothalamus volume Decreased NOR discrimination Decreased BDNF protein levels in hippocampus Decreased protein levels TRKB MWM acquisition, probe, MWM reversal (4M) Fear conditioning	Spontaneous alternation in y-maze Number of entries during y-maze task NOR discrimination Cued MWM	(Guedj et al., 2009) (Chabert et al., 2004)
	Increased brain weight Increased brain volume (P2, P7 through 6M) Increased thalamus-hypothalamus volume (4.5W-23W) Increased midbrain volume (14.5W) Increased cortex volume (2-23W) Increased hippocampal volume (9.3, 14.5, 23W)	Body weight Brain volume (P7) Midbrain volume (4.5, 9.3, 23W) Hippocampal volume (2, 4.5W)	(Sebrié et al., 2008)
TgDyrk1a	Delayed Walking activity (P14, P21) Delayed negative geotaxis (P7-P14) Delayed Climbing ability (P7) Wire suspension test (P7)	Weight/body length Sensorimotor functions Pivoting locomotion tes (P7, P10, P14, P21) Walking activity (P7, P10) Climbing activity (P10, P14) Wire suspension test (P10, P14)	(Arque et al., 2013)
	Pivoting locomotion test (P10) Walking activity (P7, P10) Homing test (P14) Wire suspension test (P14) Coat hanger test (adult)	Brain weight Sensorial & Reflexologic responses Pivoting locomotion (P7, P14) Walking activity (P14)	(Altafaj et al., 2001)

	Elevated Plus maze (adult) MWM acquisition, probe, reversal (adult)		
	Hyperactive (~2, 4 & 6M) Deficient on treadmill task (~2, 4 & 6M) Increased PPI (6-9M)	PPI (~2-3M)	(Ortiz-Abalia et al., 2008)
	Touch escape task (12-14M) Rotating rod task acquisition (12-14M) Treadmill task (3M) Irregular swimming pattern, thigmotaxic (14-16M)	SHIRPA protocol (12-14M) Gait pattern (12-14M) Accelerating rotating rod test (12-14M) Neuromuscular strength	(de Lagrán et al., 2004)
	Shorter dendrites in cortical pyramidal cells (2M) Less dendritic complexity, reduced spine density in cortical pyramidal cells (2M)	Dendrite length (P7, P10)	(De Lagran et al., 2012)
	MWM latency, thigmotaxic, probe (4M) NOR discrimination		(de la Torre et al., 2014)
	MWM acquisition, probe trial (7W) Decreased dendritic length and complexity (11W*) Cell cycle deficits, delayed neuronal differentiation, decreased cell proliferation rate (~7-11W)		(Pons-Espinal et al., 2013)
Dyrk1a +/-	Prehensile reflex (20-24M) Coat-hanger test (20-24M) Balance beam (20-24M) Walking pattern (20-24M) Accelerated rotarod test (4RPM) (20-24M) Learning efficiency index (RAWM) (20-24M)	SHIRPA protocol (20-24M) Acquisition roatarod test (20-24M) Accelerated rotarod (7, 10, 12, 24, 34RPM) (20-24M) Thickness CA3 (24M) Volume CA3 (24M)	(Arqué et al., 2008)
	Decreased dendritic complexity, dendritic length, spine density in cortical pyramidal cells (7M)		(Benavides-Piccione et al., 2005)
	Decreased body weight and length (birth into adulthood) Decreased cerebellum weight Decreased size of cerebral cortex, olfactory bulb, hypothalamus, pons, cerebellum	SHIRPA protocol	(Fotaki et al., 2002)
	Pivoting (P7) Climbing score (P14) Paw print/Gait test Decreased speed, acitivty in open field (5-7M) Coat hanger task (5-7M) Vertical grip strength (5-7M)	Pivoting (P10, P14) Walking latency (P7, P10, P14) Climbing score (P10) Wire suspension test (P10, P14) Stationary beam task (5-7M) Accelerating rod task (5-7M) Horizontal grip strength (5-7M)	(Fotaki et al., 2004)
	Decreased activity on wheel running (20-24M)		(Martinez de Lagran et al., 2007)

Supplemental Table 1: Behavioral and developmental phenotypes of transgenic *Dyrk1a* mouse models. Abbreviations: MWM (Morris Water Maze), M (Month), P (Postnatal Day), LTP (Long Term Potentiation), LTD (Long Term Depression), PFC (Prefrontal Cortex), PPI (Pre-Pulse Inhibition), PFC (Prefrontal Cortex), NOR (Novel Object Recognition)

Age	Sex	Type of Tissue	Level of Expression	Authors
P30	male and female	Cerebral Cortex	High	(Lizio et al., 2015)
Adult	male	Cerebral Cortex	High	(Lizio et al., 2015)
P30	male and female	cerebellum	High	(Lizio et al., 2015)
Adult	male	Cerebellum	Low	(Lizio et al., 2015)
P77	male	Brain	High	(Soumillon et al., 2013)
PD75	male and female	Brain	High	(Barbosa-Morais et al., 2012)
Adult	male	Dentate Gyrus	Low	(Ramos et al., 2013)
P0	male and female	Hippocampus	High	(Lizio et al., 2015)
Adult		Hippocampus	Medium	(Keane et al., 2011)
Adult	male	Hippocampus	Low	(Lizio et al., 2015)

Supplemental Table 2: Gene expression of *Dyrk1a* in brain regions at various ages in mice. Data was compiled from the EMBL-EBI Expression Atlas

	P0	P2	P6	P14-adulthood	P30	P45	P112	P120 - onward
Deficient Phenotype	reduced number of mitotic GCP (3)	reduced cerebellum volume (9)	Smaller cerebellar size (3)	IGL thinner (3)	Fewer labeled cells in the IGL (9)	reduced cerebellar volume (5)	Decreased cerebellar area, GC density (11)	Reduced cerebellar volume (10)
		EGL volume and total number of GCP in the EGL were smaller; fewer BrdU labeled cells (9)	GC density in IGL is reduced (3)		Smaller percentage of BrdU and NeuN cells (9)	Increased GC surface area (12)		Reduced density of GC's and PC's (10)
		Higher rates of apoptosis (based on appearance) (9)	Reduced number of mitotic figures in EGL (3)					Decreased IGL, ML area (10)
		Longer cell cycle; specifically at G1 and G2 phase (9)	Reduced GCP and mitotic cells (3)					
		Reduced thickness of the external and interal granular layers, cell denisty in the exteranl granular, purkinje cell and internal granular layers; cerebellar lobes had shallower fissures (5)						
Preserved Phenotype	Cerebellum same size (3)	No differences in S or M phase length (9)	No differences in apoptosis (3)					
	Number of GCP (3)							
	Normal B-galactosidase activity (3)							

Supplemental Table 3: Anatomical and histological cerebellar phenotypes in Ts65Dn mice. Abbreviations: GCP (Granule Cell Precursors), IGL (Internal Granular Layer), EGL (External Granule Layer), ML (Molecular Layer)

Sources: 1) (Najas et al., 2015); 2) (Chakrabarti et al., 2007); 3) (Roper et al., 2006); 4) (Contestabile et al., 2007); 5) (Guidi et al., 2014); 6) (Lorenzi and Reeves, 2006); 7) (Bianchi et al., 2010); 8) (Clark et al., 2006); 9) (Contestabile et al., 2009); 10) (Baxter et al., 2000); 11) (Das et al., 2013); 12) (Usowicz and Garden, 2012)

	E13.5-E18.5	P2	P6	P8	P15	P18	P30	P45	2-5 Months	5 months+
Deficient Phenotype		fewer cells in granule cell layer, hillus and molecular layer (4)	Fewer granule cells in DG; lower granule cell density; fewer mitotic cells (6)	decreased levels of SY38 and PSD95 protein in hippocampus and cortex (2)	proliferation in the SGZ and SVZ (7)	Ts6Dn had fewer cells in the hillus (2)	Fewer cells only in the granule cell layer (2)	Reduced Volume; Fewer Ki67 cells in SVZ & SGZ (7)	Ts65Dn showed proliferation deficits (8)	Mean neuron number was decreased in DG, higher in CA3 (14)
	in CA3, longer cell cycle (2)	volume of granule cell layer was smaller in Ts65Dn mice (4)		fewer PSD95 synapses in CA3, no differences in SY38 (2)	Fewer apoptotic cells in the DG, and a similar number in the SVZ (measured using cells that express caspase-3) (7)		More cells with an astrocytic phenotype (4)	higher levels of P45, reduced levels of phosphorylated Erk1/2 (5)	Ts65Dn mice showed fewer clusters of cells (8)	12-13month old Ts65Dn presented reduced DG volume, SGZ area, number of granule neurons, and number of BrdU positive cells (16)
	reduced hippocampal thickness (2)	Ts65Dn mice had larger percent number of cells in G2 phase, smaller percent in M phase (4)		fewer PSD95 & SY38 synapses in CA1 (2)	Granule cell layer had a smaller volume, reduced granule cell density and reduced number of granule cells (7)		Smaller number of granule cells & GC density (4)	Fewer BrdU cells, NeuN/BrdU labeled cells, astroctyes, reduced cell density, cell survival deficits (7)	fewer granule cells in DG; reduced volume of GCL (8)	16-23month old Ts65Dn presented decreased neuronal density in CA1, total synapse density in DG (17)
		reduced volume of granule cell layer, reduced granule cell density and reduced number of granule cells; reduced volume of CA3 & CA1, reduced pyramidal cell density and reduced number of pyramidal neurons (5)			lower expression of 5-Ht1A receptor in hippocampus (7)		Decreased BrdU and NeUN labeled cells in DG (22)	Smaller granule cell layer volume, reduced granule cell density, reduced granule cell number in Ts mcie (7)	Fewer GC’s in DG (11)	13-17month old Ts65Dn presented fewer DCX positive cells (18)
		Ts mice have reduced expression of 5-HT1A-R in DG and SVZ (5)			BDNF expression is lower in hippocampus of Ts mice, as well as NGF expression (7)			Dendritic trees with reduced length and fewer branches (5)	Reduced LTP, increased LTD (13)	13-15month old Ts65Dn present reduced cell proliferation and density of surviving cells (21)
		Ts mice have reduced proliferation in DG (5)			Higher 5HT metabolite concentration (7)			Reduced protein levels of SYN and PSD95; also reduction in immunoreactivity (5)	Deficits in LTP (15,20)	
								Decreased BrdU and NeUN labeled cells in DG (22)		
Preserved Phenotype		no differences in apoptotic cell death (4)	no differences in GCL or PCL; pyramidal cells or density of pyramidal cells; no differences in apoptosis in DG; similar mitotic index (6)		5-HT concentration (7)	# of cells in granule cell layer (4)	No differences in cells with neuronal phenotype (4)		no differences in number of pyramidal cells in PCL; no volume differences in PCL; or granule and pyramidal cell densities; no differences in number of pyramidal cells in either CA1 or CA3; similar volumes and neuronal densities in CA1, CA3 and DG (6)	Hippocampal volumes no different than controls (except for CA2) (14)
						no differences in apoptotic cell death (4)	no difference in volume of granule cell layer (4)		No differences in HFS-induced LTP (15)	At 2-3, 6, 12, 16 and 21 months, no differences in brain weight (19)

						At P22, no differences in brain weight (19)			No differences in number of proliferating or surviving cells (21)	

Supplemental Table 4. Anatomical and histological hippocampal phenotypes in Ts65Dn mice. Abbreviations: GCL (Granule Cell Layer), PCL (Pyramidal Cell Layer), GC (Granule Cell), SVZ (Subventricular Zone), DG (Dentate Gyrus). Sources: 1) (Najas et al., 2015); 2) (Chakrabarti et al., 2007); 3) (Roper et al., 2006); 4) (Contestabile et al., 2007); 5) (Guidi et al., 2014); 6) (Lorenzi and Reeves, 2006); 7) (Bianchi et al., 2010); 8) (Clark et al., 2006); 9) (Contestabile et al., 2009); 10) (Baxter et al., 2000); 11) (Das et al., 2013); 12) (Usowicz and Garden, 2012); 13)(Siarey et al., 1999); 14) (Insausti et al., 1998); 15) (Costa and Grybko, 2005); 16) (Llorens-Martin et al., 2010); 17) (Kurt et al., 2004); 18) (Velazquez et al., 2013); 19) (Belichenko et al., 2004); 20) (Kleschevnikov et al., 2004); 21) (Rueda et al., 2005); 22) (Chakrabarti et al., 2011)

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