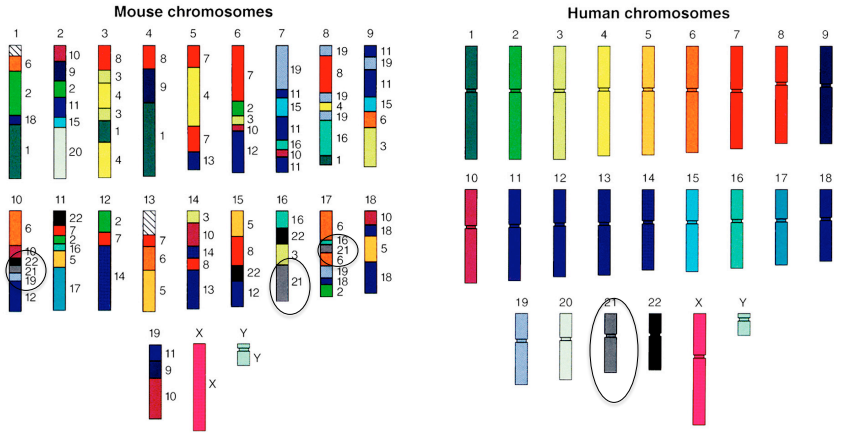
Mouse and Human Genetic Similarities



Neural Plasticity 3

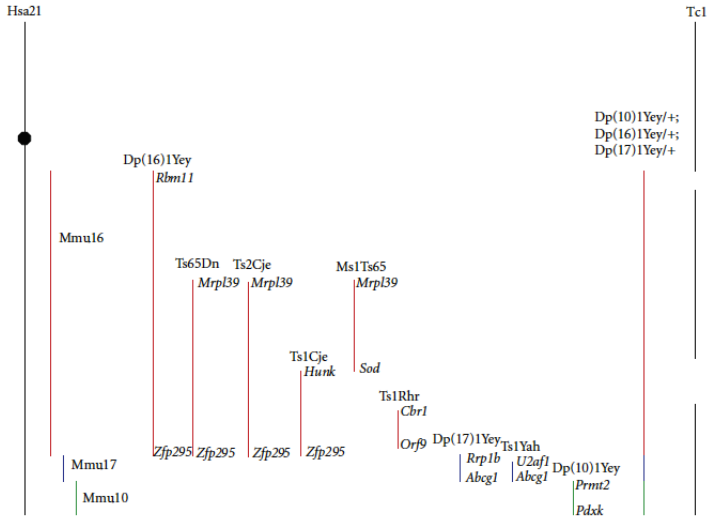


FIGURE 1: Schematic representation of Hsa21 and syntenic regions of Mmu16, Mmu17, and Mmu10 and the different mouse models trisomic for different sets of genes orthologous to those of Hsa21. The flanking genes found at the boundaries of the triplicated region in each model are written in italics. Modified from [3, 137].

Table 1: Behavioural and cognitive alterations in DS and in the different DS mouse models.

Trisomy	Hsa21	Segment of Mmu16						Segment of Mmu17		Segment of Mmu10	Segment of Mmu16, Mmu17, and Mmu10	Hsa21
	DS	Dp(16)1Yey/+	Ts65Dn	Ts2Cje	Ts1Cje	Ms1Ts65	Ts1Rhr	Dep(17)1Yey/+	Ts1Yah	Dp(10)1Yey/+	Dp(10)1Yey/+; Dp(16)1Yey/+; Dep(17)1Yey/+ Yu et al., 2010	Tc1
Motor skills	Delayed acquisition		Delayed acquisition									
Motor coordination	Impaired		Impaired									Impaired
Activity and attention	Reduced attention		Hyperactivity and reduced attention		Normal activity	Normal activity	Normal activity					Increased spontaneous activity
Context discrimination		Impaired	Impaired					Unchanged		Unchanged	Impaired	
Spatial learning and memory	Impaired	Impaired	Impaired		Impaired	Impaired		Unchanged	Enhanced	Unchanged	Impaired	Impaired
Working and reference memory	Impaired		Impaired									Impaired
Novel object recognition			Impaired				Impaired		Impaired			
Operant conditioning			Impaired									

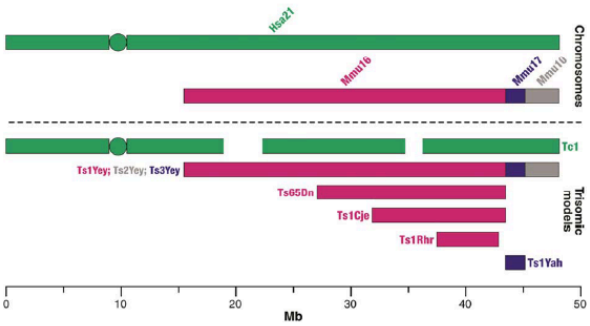
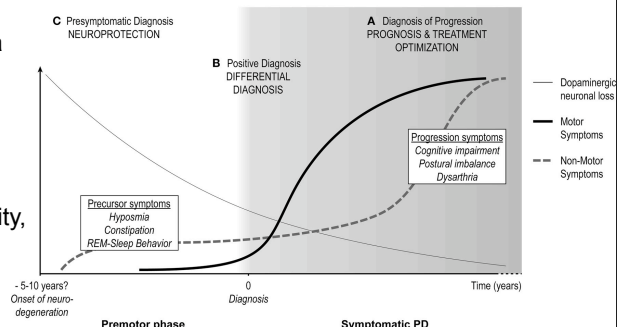


Figure 1 Mouse models of Down syndrome. HSA21 is syntenic with three regions on the mouse genome: mouse chromosomes 16 (Mmu16), 17 (Mmu17) and 10 (Mmu10). The Tc1 mouse model carries a freely segregating copy of HSA21 and is trisomic for 80% of HSA21 genes [O'Doherty et al., 2005]. The Ts1Yey;Ts2Yey;Ts3Yey mouse model is trisomic for all mouse orthologs of HSA21 genes [Yu et al., 2010b) and was developed by breeding Ts1Yey, Ts2Yey, and Ts3Yey segmentally trisomic models [Yu et al., 2010a]. The Ts65Dn mouse model is the most commonly used DS mouse model and is segmentally trisomic for approximately 104 genes on Mmu16 [Reeves et al., 1995]. Other segmentally trisomic models for Mmu16 include Ts1Cje, which contains approximately 81 of the trisomic genes on the Ts65Dn mouse model [Sago et al., 1998], and Ts1Rhr, which encodes 33 genes that have conserved synteny with genes in the human "Down syndrome critical region" [Olson et al., 2004]. The Ts1Yah mouse model is segmentally trisomic for Mmu17 and contains 12 genes found on the HSA21 sub-telomeric region [Pereira et al., 2009]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Mouse Model	Behavioral Tests	Brain Anatomy	Neurodegeneration and AD
Ts65Dn	Impaired performance in MWM [Reeves et al., 1995); Impaired performance in NORT [Fernandez et al., 2007].	Altered brain shape and reduced cerebellar volume [Aldridge et al., 2007]; Reduced density of cerebellar granule cells [Contestabile et al., 2009].	BFCN neurodegeneration [Granholm et al., 2000]; Enlarged early endosomes [Cataldo et al., 2003]; Severely impaired NGF retrograde axonal transport [Salehi et al., 2006]; Degeneration of locus coeruleus neurons [Salehi et al., 2009].
Ts1Cje	Impaired performance in MWM [Sago et al., 1998]; No deficits in NORT [Belichenko et al., 2007].	Smaller brains, hypoplasia of cerebellum and enlarged ventricles [Ishihara et al., 2009]; Reduced density of cerebellar granule cells [Moldrich et al., 2009]; Elevated neuronal apoptosis [Micali et al., 2010].	No BFCN neurodegeneration [Sago et al., 1998]; No enlargement of early endosomes [Cataldo et al., 2003]; Moderately impaired NGF retrograde axonal transport [Salehi et al., 2006]; Hyperphosphorylation of tau [Shukkur et al., 2006].
Ts1Rhr	No deficits in MWM [Olson et al., 2007]; Impaired performance in NORT [Belichenko et al., 2009].	Altered brain shape but normal cerebellum volume [Olson et al., 2007].	Not available.
Tc1	Impaired spatial working memory in MWM [Morice et al., 2008]; Short-term impairments in NORT [Morice et al., 2008].	Reduced density of cerebellar granule cells [O'Doherty et al., 2005].	Not available.
Ts1Yey; Ts2Yey; Ts3Yey	Impaired performance in MWM [Yu et al., 2010b].	Not available.	Not available.
Ts1Yey	Impaired performance in MWM [Yu et al., 2010a].	Not available.	Not available.
Ts2Yey	No deficits in MWM [Yu et al., 2010b].	Not available.	Not available.
Ts3Yey	No deficits in MWM [Yu et al., 2010b].	Not available.	Not available.
Ts1Yah	Enhanced performance in MWM [Pereira et al., 2009].; Impaired performance in NORT [Pereira et al., 2009].	Not available.	Not available.

Parkinson's disease (PD, also called Parkinsons "chorea") is a degenerative disorder of CNS that impairs *motor skills and speech (movement disorder or "chorea")*.

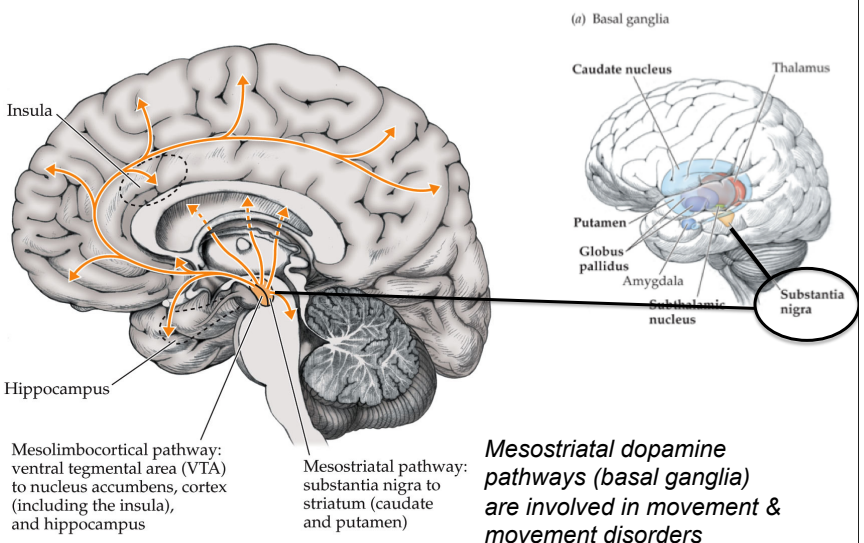
Symptoms include muscle rigidity, tremor, a slowing of movement (bradykinesia) and later, a loss of movement (akinesia).



Parkinson's is caused by decreased stimulation of the motor cortex by the *basal ganglia* and particularly the ***substantia nigra*** (a MIDBRAIN structure), Resulting from ***dopamine depletion***.

Later 2nd symptoms may include high level cognitive dysfunction & language problems (*PD dementia*).

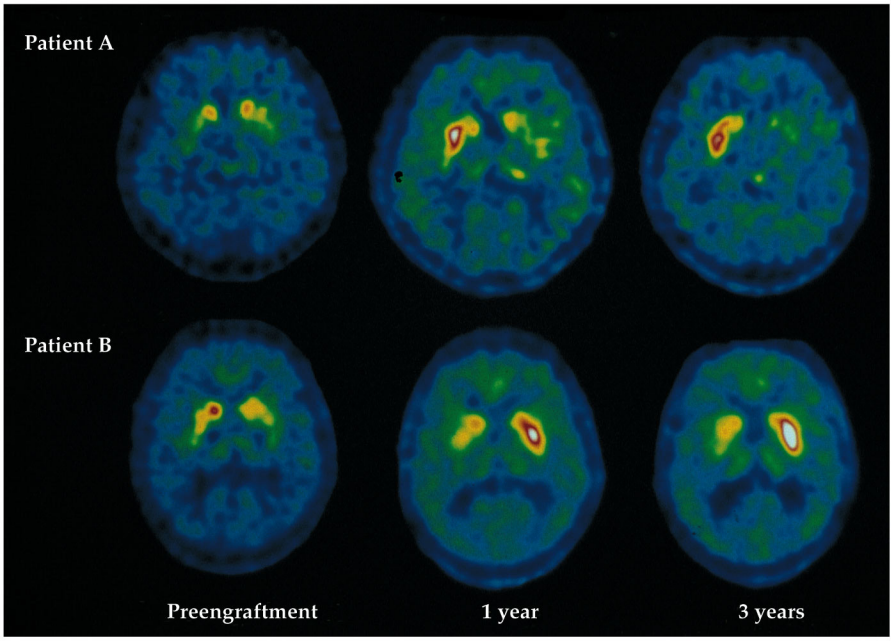
Parkin's Disease and Depletion of Dopaminergic Pathways in the Basal Ganglia



(Cortico-limbic dopamine pathways are involved in drug abuse and emotion, to be discussed tues).

*Mesostriatal dopamine pathways (basal ganglia) are involved in movement & movement disorders (e.g., **Parkinsons disease**).*

Figure 11.22 Brain Implants to Treat Parkinson's Disease



***Biological Psychology 6e*, Figure 11.22**