Supplementary Table 1 – Neurotransmitter deficits in Frontotemporal Lobar Degeneration Syndromes

Neurotransmitter	Frontotemporal dementia	Reference	Progressive supranuclear palsy	Reference	Corticobasal syndrome	Reference
Dopamine						
Nigrostriatal pathway	Reduced dopaminergic neurons	(Rinne *et al.*, 2002) (Sedaghat *et al.*, 2007) (Pal *et al.*, 2001) (Gil-Navarro *et al.*, 2013)	Reduced dopaminergic neurons	(Hardman *et al.*, 1997) (Oyanagi *et al.*, 2001) (Warren *et al.*, 2007) (Baron *et al.*, 1986) (Im *et al.*, 2006) (Oh *et al.*, 2012)	Neuronal loss in substantia nigra and striatum	(Oyanagi *et al.*, 2001) (Pirker *et al.*, 2015) (Klaffke *et al.*, 2006) (Laureys *et al.*, 1999) (Sawle *et al.*, 1991) (Nagasawa *et al.*, 1996)
	Low dopamine levels	(Kanazawa *et al.*, 1988) (Nagaoka *et al.*, 1995)	Low dopamine levels	(Ruberg *et al.*, 1985) (Hornykiewicz and Shannak, 1994)	Dopaminergic neuron loss not seen in all patients	(Cilia *et al.*, 2011) (Chaal and Rowe, 2013) (Kaasinen *et al.*, 2013)
			Reduced D2 receptors in the striatum	(Brooks *et al.*, 1992) (Arnold *et al.*, 2002) (Oyanagi, 2002) (Pascual *et al.*, 1992)	D2 receptor levels are unaffected	(Klaffke *et al.*, 2006) (Pirker *et al.*, 2013)
			Preserved D1 receptors	(Pierot *et al.*, 1988)		
Mesocortical pathway	Reduced D2 dopamine receptors	(Frisoni *et al.*, 1994)	Reduced dopaminergic neurons	(Murphy *et al.*, 2008)	Reduced dopaminergic neurons	(Sawle *et al.*, 1991)
	CSF dopamine reduced in some but not all studies	(Sjogren *et al.*, 1998) (Vermeiren *et al.*, 2013)	Loss of D2 receptors in the frontal cortex	(Ruberg *et al.*, 1985)		
Noradrenaline						
	Minimal neuronal loss in	(Yang and Schmitt,	Neuronal loss in the locus	(Hauw *et al.*, 1994)	Tau pathology in the	(Dickson, 1999)

	the locus coeruleus	2001) (Brunnström *et al.*, 2011)	coeruleus	(Mori *et al.*, 2002) (Dickson *et al.*, 2010)	locus coeruleus	
	Noradrenaline levels normal or high in the cerebral cortex	(Vermeiren *et al.*, 2016)	Reduced levels of noradrenaline in the caudate and putamen	(Hornykiewicz and Shannak, 1994)		
	CSF noradrenaline correlates with disease severity	(Engelborghs *et al.*, 2008)				
Serotonin						
	Loss of neurons and tau deposition in the raphe nucleus	(Yang and Schmitt, 2001) (Irwin *et al.*, 2016)	Tau deposition in the raphe nucleus	(Revesz *et al.*, 1996)	Neuronal loss in the raphe nucleus	(Gibb *et al.*, 1989)
	Serotonin transporter gene variants affect brain atrophy and clinical presentation	(Albani *et al.*, 2008) (Yokoyama *et al.*, 2015) (Premi *et al.*, 2015)	Serotonergic neurons reduced in the caudate and frontal and temporal lobes	(Chinaclia and Landwehrmeyer, 1993)		
	Serotonin levels normal or elevated at *post mortem*	(Bowen *et al.*, 2008) (Vermeiren *et al.*, 2016)	Serotonin levels not significantly reduced	(Hornykiewicz and Shannak, 1994)		
	5HT1A and 2A receptors reduced in the midbrain, frontal and temporal lobes	(Sparks and Markesbery, 1991) (Francis *et al.*, 1993) (Procter *et al.*, 1999) (Bowen *et al.*, 2008) (Franceschi *et al.*, 2005) (Lanctôt *et al.*, 2007)	5HT1B and 2A are upregulated in the basal ganglia	(Castro *et al.*, 1998) (Stamelou *et al.*, 2009)		
	CSF serotonin levels unchanged but HVA/5HIAA levels correlate with aggressive behaviour	(Vermeiren *et al.*, 2016) (Engelborghs *et al.*, 2008)				

Acetylcholine						
	Reduced cholinergic neurons in the nucleus basalis	(Sparks and Markesbery, 1991)	Loss of cholinergic neurons in nucleus basalis, selected midbrain nuclei and pedunculopontine nucleus	(Jellinger, 1988) (Kasashima and Oda, 2003) (Javoy-Agid, 1994) (Juncos *et al.*, 1991)	Loss of cholinergic neurons in nucleus basalis	(Kasashima and Oda, 2003)
			Pre synaptic cholinergic neurons reduced in the nucleus basalis, putamen, caudate and pallidum.	(Ruberg *et al.*, 1985) (Javoy-Agid, 1994) (Suzuki *et al.*, 2002) (Mazere *et al.*, 2012) (Shinotoh *et al.*, 1999) (Gilman *et al.*, 2010) (Hirano *et al.*, 2010)		
	No evidence of cholinergic neuron loss in the cerebral cortex	(Wood *et al.*, 1983) (Hirano *et al.*, 2010) (Procter *et al.*, 1999) (Hansen *et al.*, 1988)	Loss of cholinergic neurons in cerebral cortex	(Ruberg *et al.*, 1985) (Javoy-Agid, 1994) (Hirano *et al.*, 2010)	Reduced cholinergic neurons in the frontal, parietal and occipital cortex	(Hirano *et al.*, 2010)
	Conflicting results on cholinergic receptors	(Weinberger *et al.*, 1991) (Wood *et al.*, 1983) (Procter *et al.*, 1999)	No change in muscarinic receptor density	(Ruberg *et al.*, 1985) (Asahina *et al.*, 1998)		
	Atrophy of cholinergic basal nuclei in PPA	(Teipel *et al.*, 2016)				
Glutamate						
	Glutamatergic neurons	(Ferrer, 1999)	Glutamatergic neurons	(Henderson *et al.*,	No evidence	

	reduced in the thalamus, frontal and temporal cortex		reduced in the basal ganglia	2000)		
	Glutamate levels reduced in the frontal and temporal lobes	(Ernst *et al.*, 1997) (Sarac *et al.*, 2008)	NMDA receptors unchanged in the frontal and temporal lobes	(Holemans *et al.*, 1991)		
	AMPA and NMDA receptor levels reduced in the frontal and temporal lobes	(Francis *et al.*, 1993) (Procter *et al.*, 1999) (Bowen *et al.*, 2008)				
	Metabotropic glutamate receptors reduced in the cerebral cortex, basal ganglia and thalamus	(Leuzy *et al.*, 2016)				
GABA						
	GABAergic neurons reduced in the frontal and temporal lobes	(Ferrer, 1999)	GABAergic neurons reduced in the basal ganglia	(Levy *et al.*, 1995)	No evidence	
	GABA levels reduced in the basal ganglia	(Kanazawa *et al.*, 1988)	GABA receptors binding reduced	(Landwehrmeyer and Palacios, 1994) (Suzuki *et al.*, 2002) (Foster *et al.*, 2000)		

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