eFigure Legends

eFigure 1. Change in number of depressive symptoms on the Center for Epidemiological Studies Depression scale.

eFigure 2. Relation of brainstem tangle density to depressive symptoms in persons with no (green) and mild (orange) cognitive impairment, adjusted for age at death, sex, and education.

eFigure 3. Distributions of aminergic neuronal density in brainstem nuclei.

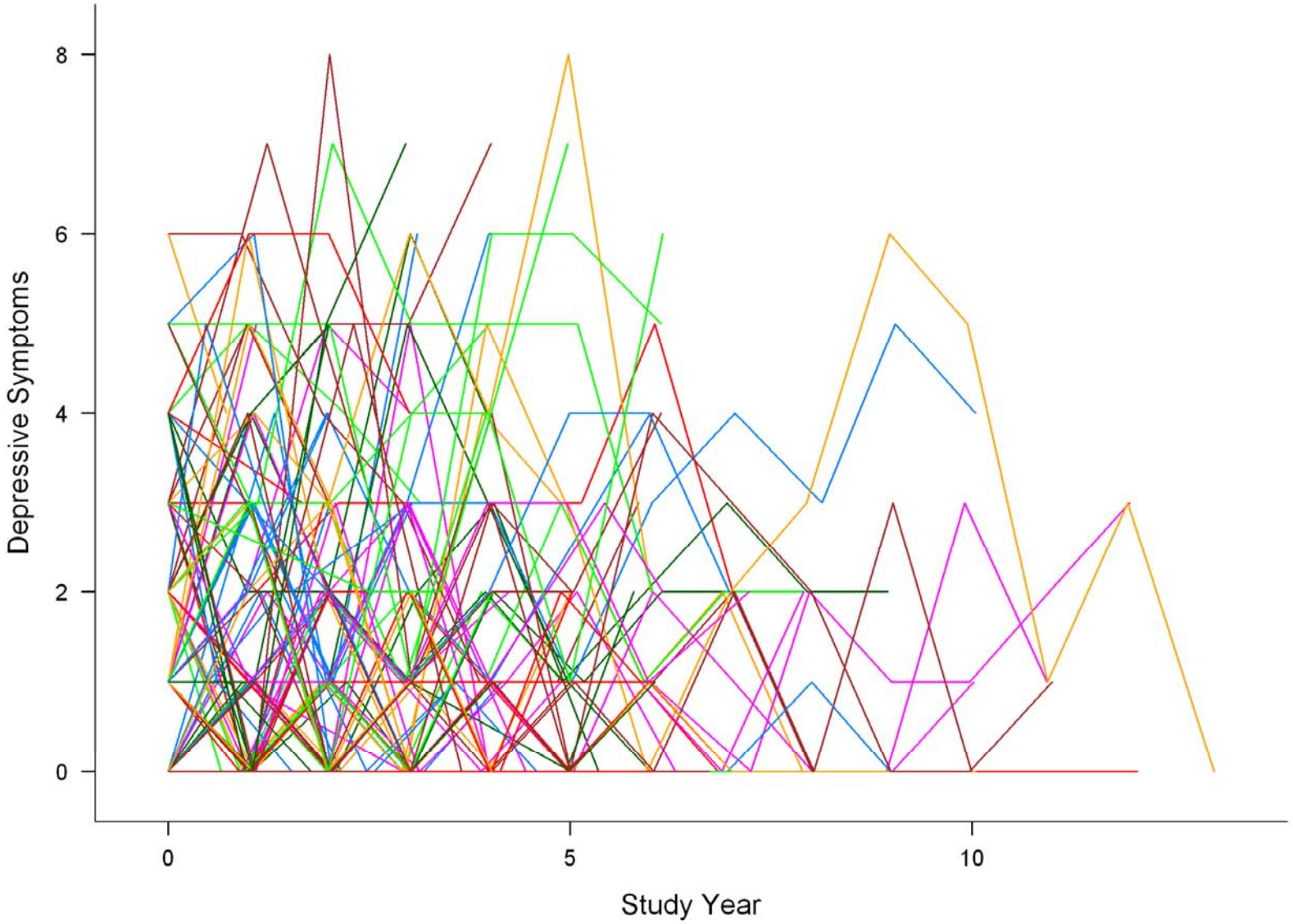
eTable 1. Antidepressant medication use in 40 participants[a]

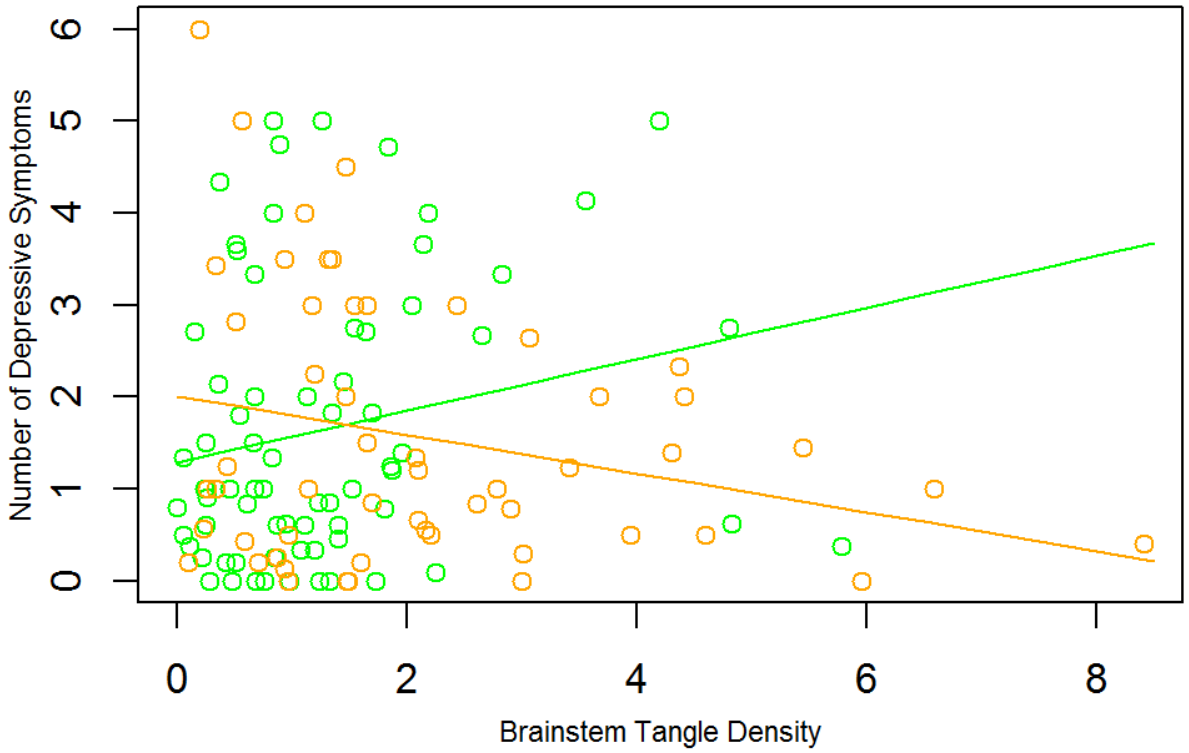
Antidepressant Class	Medication	Number of participants
Selective norepinephrine reuptake inhibitor	duloxetine	1
	venlafaxine	5
Selective serotonin reuptake inhibitor	citalopram	2
	escitalopram	8
	fluoxetine	1
	paroxetine	9
	sertraline	21
Tetracyclic	mirtazapine	7
Tricyclic	amitriptyline	7
	nortriptyline	1

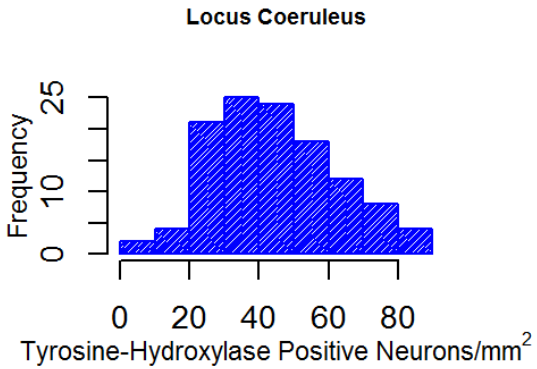
[a] Number of participants who used a medication at least once during the observation period.

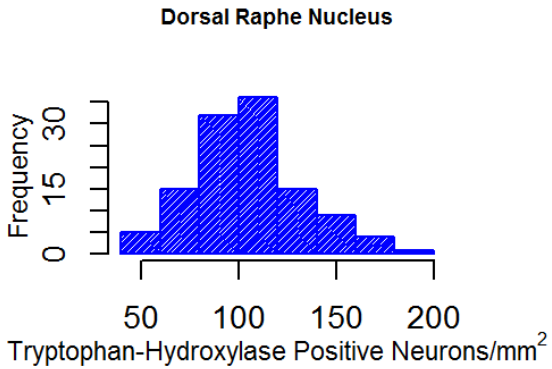
eTable 2. Relation of demographic and postmortem variables to density of aminergic neurons in brainstem nuclei*

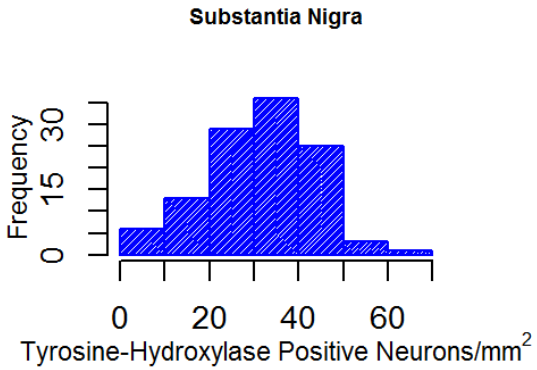
Covariate	Locus Coeruleus	Dorsal Raphe Nucleus	Substantia Nigra	Ventral Tegmental Area
Age at death	r = -0.09, p = 0.33	r = 0.08, p = 0.40	r = -0.12, p = 0.20	r = -0.18, p= 0.061
Sex	t[116] = -0.06, p = 0.52	t[115] = -0.4, p = 0.70	t[111] = -0.9, p = 0.37	t[109]= -1.4, p=0.16
Education	r = 0.14, p = 0.12	r = 0.02, p = 0.80	r = 0.03, p = 0.72	r = 0.03, p = 0.75
Last evaluation, months	r = -0.10, p = 0.30	r = -0.08, p = 0.39	r = -0.02, p = 0.87	r = 0.01, p = 0.89
Postmortem interval, hours	r = 0.04, p = 0.64	r = -0.12, p = 0.21	r = -0.23, p = 0.02	r = -0.03, p = 0.73
pH	r = 0.14, p = 0.13	r = 0.11, p = 0.23	r = 0.23, p = 0.02	r = 0.01, p = 0.91
Brainstem Lewy bodies	r = -0.06, p = 0.52	r = 0.08, p = 0.41	r = -0.21, p = 0.02	r = -0.19, p = 0.046
Brainstem tangles	r = 0.04, p = 0.65	r = 0.13, p = 0.17	r = 0.09, p = 0.32	r = 0.02, p = 0.84

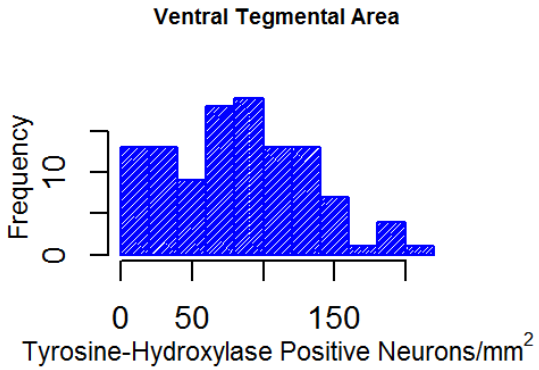

Depressive Symptoms
8
6
4
2
0
0
5
10
Study Year


Number of Depressive Symptoms
0
1
2
3
4
5
6
0
2
4
6
8
Brainstem Tangle Density


Locus Coeruleus
Frequency
0
10
25
0
20
40
60
80
Tyrosine-Hydroxylase Positive Neurons/mm2


Dorsal Raphe Nucleus
Frequency
0
15
30
50
100
150
200
Tryptophan-Hydroxylase Positive Neurons/mm2


Substantia Nigra
Frequency
0
15
30
0
20
40
60
Tyrosine-Hydroxylase Positive Neurons/mm2


Ventral Tegmental Area
Frequency
0
10
0
50
150
Tyrosine-Hydroxylase Positive Neurons/mm2