



Neurobiology of suicidal behaviour

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- approaches to the neurobiological study of suicidal behaviour
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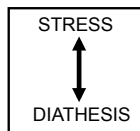
Multiple causes of suicidal behaviour

Distal

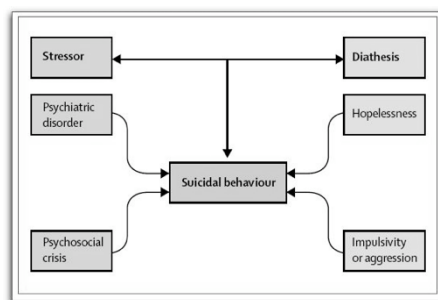
genetic load
limited foetal growth / perinatal circumstances
adverse early life events
neurobiological disturbances (eg 5-HT, HPA)
personality characteristics
cognitive psychology
impulsivity, aggression

Proximal

psychiatric disorders
somatic disorders
psychosocial stressors
availability of methods

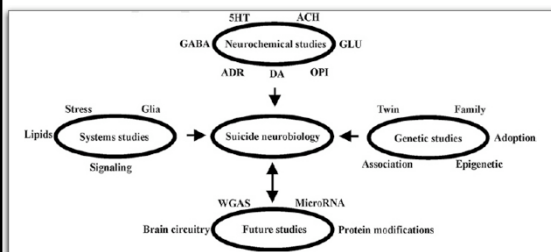


Stress-diathesis interaction model of suicidal behaviour



Hawton & van Heeringen, 2009

Neurobiology of suicidal behaviour: study approaches



Ernst et al 2009

The association between brain-derived neurotrophic factor polymorphism (BDNF Val66Met) and suicide

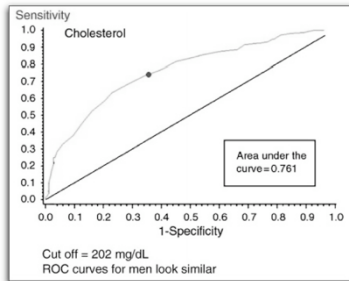
Peter Pregelj^a, Gordana Nedic^b, Alja Videtič Paska^c, Tomaž Zupanc^d, Matea Nikolac^b, Jože Balazic^d, Martina Tomori^a, Radovan Komel^e, Dorotea Muck Seler^f, Nela Pivac^{b, g, h}

	BDNF Val66Met Genotypes		Alleles		Met carriers		Val/Val N (%)
	Val/Val N (%)	Val/Met N (%)	Val N (%)	Met N (%)	Val/Met + Met/Met N (%)	Val/Met N (%)	
Male: Control group	80 (36.7)	49 (36.6)	5 (3.7)	209 (78.0)	59 (22.0)	54 (40.3)	80 (36.7)
Suicide victims	172 (63.2)	88 (32.4)	12 (4.4)	432 (79.4)	112 (20.6)	100 (36.8)	172 (63.2)
	$\chi^2 = 0.752$; $p = 0.683$; power = 0.107			$\chi^2 = 0.220$; $p = 0.639$; power = 0.063		$\chi^2 = 0.476$; $p = 0.490$; power = 0.084	
Suicide victims - Violent	145 (63.6)	72 (31.6)	11 (4.8)	362 (79.4)	94 (20.6)	83 (36.4)	145 (63.4)
- Non-violent	27 (61.4)	16 (36.3)	1 (2.3)	70 (79.5)	18 (20.5)	17 (38.6)	27 (61.4)
	$\chi^2 = 0.830$; $p = 0.659$; power = 0.113			$\chi^2 = 0.000$; $p = 0.973$; power = 0.000		$\chi^2 = 0.080$; $p = 0.779$; power = 0.049	
Female: Control group	48 (71.6)	15 (22.4)	4 (6.0)	59 (72.0)	23 (28.0)	15 (28.4)	48 (71.6)
Suicide victims	47 (54.0)	35 (40.2)	5 (5.8)	129 (74.1)	45 (25.9)	40 (46.0)	47 (54.0)
	$\chi^2 = 5.619$; $p = 0.060$; power = 0.049			$\chi^2 = 0.048$; $p = 0.827$; power = 0.052		$\chi^2 = 4.972$; $p = 0.026$; power = 0.579	
Suicide victims - Violent	37 (52.9)	28 (40.0)	5 (7.1)	102 (72.9)	38 (27.1)	33 (47.1)	37 (52.9)
- Non-violent	10 (58.8)	7 (41.2)	0 (0)	27 (79.4)	7 (20.6)	7 (41.2)	10 (58.8)
	$\chi^2 = 1.308$; $p = 0.520$; power = 0.153			$\chi^2 = 0.610$; $p = 0.434$; power = 0.082		$\chi^2 = 0.200$; $p = 0.658$; power = 0.050	

Pregelj et al 2011

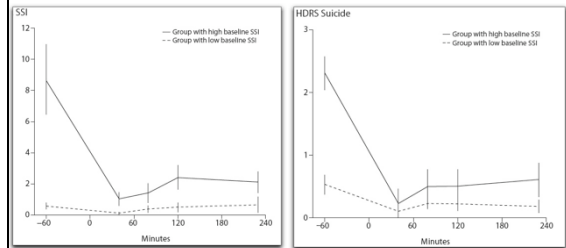
Measurement of total serum cholesterol in the evaluation of suicidal risk

Emilie Oli  ^{a,b,c}, Marie Christine Picot^{a,b}, S  bastien Guillaume^{a,b,c},
Mocrane Abbar^d, Philippe Courtet^{a,b,c,*}



Oli   et al 2011

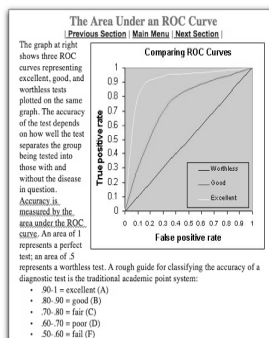
Rapid Resolution of Suicidal Ideation After a Single Infusion of an *N*-Methyl-D-Aspartate Antagonist in Patients With Treatment-Resistant Major Depressive Disorder



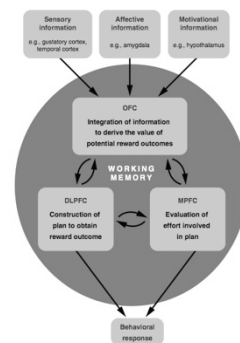
DiazGranados et al 2010

Conclusions

- Increasing number of approaches to the neurobiological study of suicidal behaviour
- Increasing support for
 - stress-diathesis model
 - role of gene-environment interaction
- Involvement of number of neurochemical systems (including 5-HT, GLU and GABA) and particular brain areas (including OFC and DLPFC)
- Clinical relevance of findings is increasing
- Further study needed to identify biomarkers and develop targeted treatments

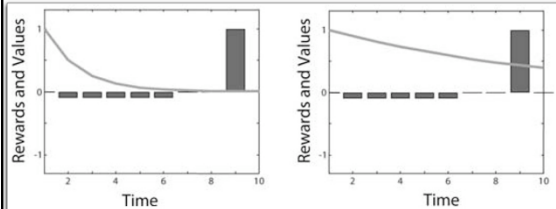


Prefrontal cortex



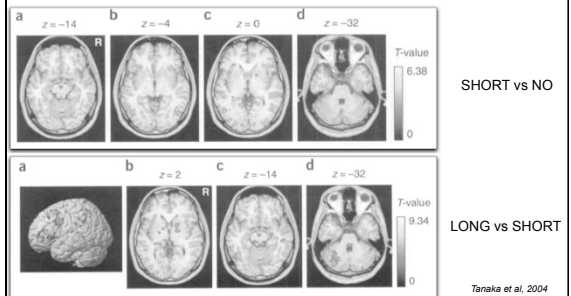
Wallis, 2007

Serotonin and the Evaluation of Future Rewards



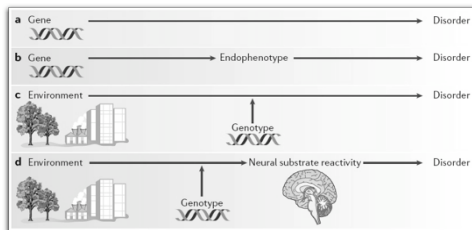
Schweighofer et al., 2007

Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops



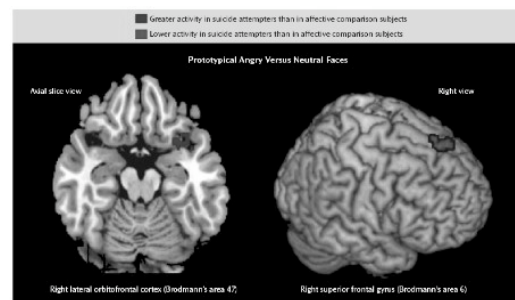
Tanaka et al., 2004

Neurobiology of suicidal behaviour: gene/environment approaches



Caspi & Moffit, 2006

Orbitofrontal cortex response to angry faces in men with histories of suicide attempts

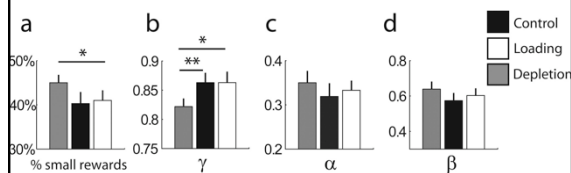


Jollant et al., 2008

4528 • The Journal of Neuroscience, April 23, 2008 • 28(17):4528–4532

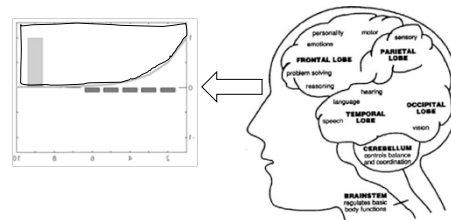
Brief Communications

Low-Serotonin Levels Increase Delayed Reward Discounting in Humans

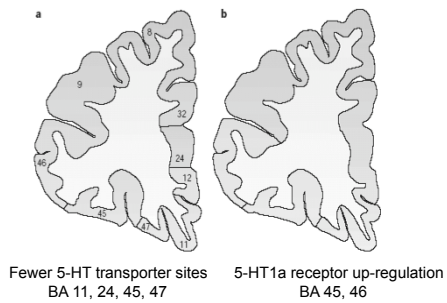


Schweighofer et al., 2008

Is serotonin-dependent myopia for the future the missing link between depression and suicide?



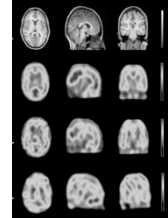
Changes in serotonergic functioning: post-mortem findings (Mann, 2003)



Prefrontal 5-HT_{2a} receptor binding index, hopelessness and personality characteristics in attempted suicide

	Binding Potential (Spearman r)	Hopelessness (Spearman r)
TCI-scores		
Novelty seeking	-0.01	-0.28
Harm avoidance	-0.57 *	0.84 ***
Reward dependence	0.45	-0.49
Self-Directedness	0.53 *	0.24
Cooperativeness	0.54 *	-0.57 *
Self-Transcendence	-0.22	-0.71 **
Hopelessness	-0.54 *	

* p < .05; ** p < .01; *** p < .001



Van Heeringen et al, 2003