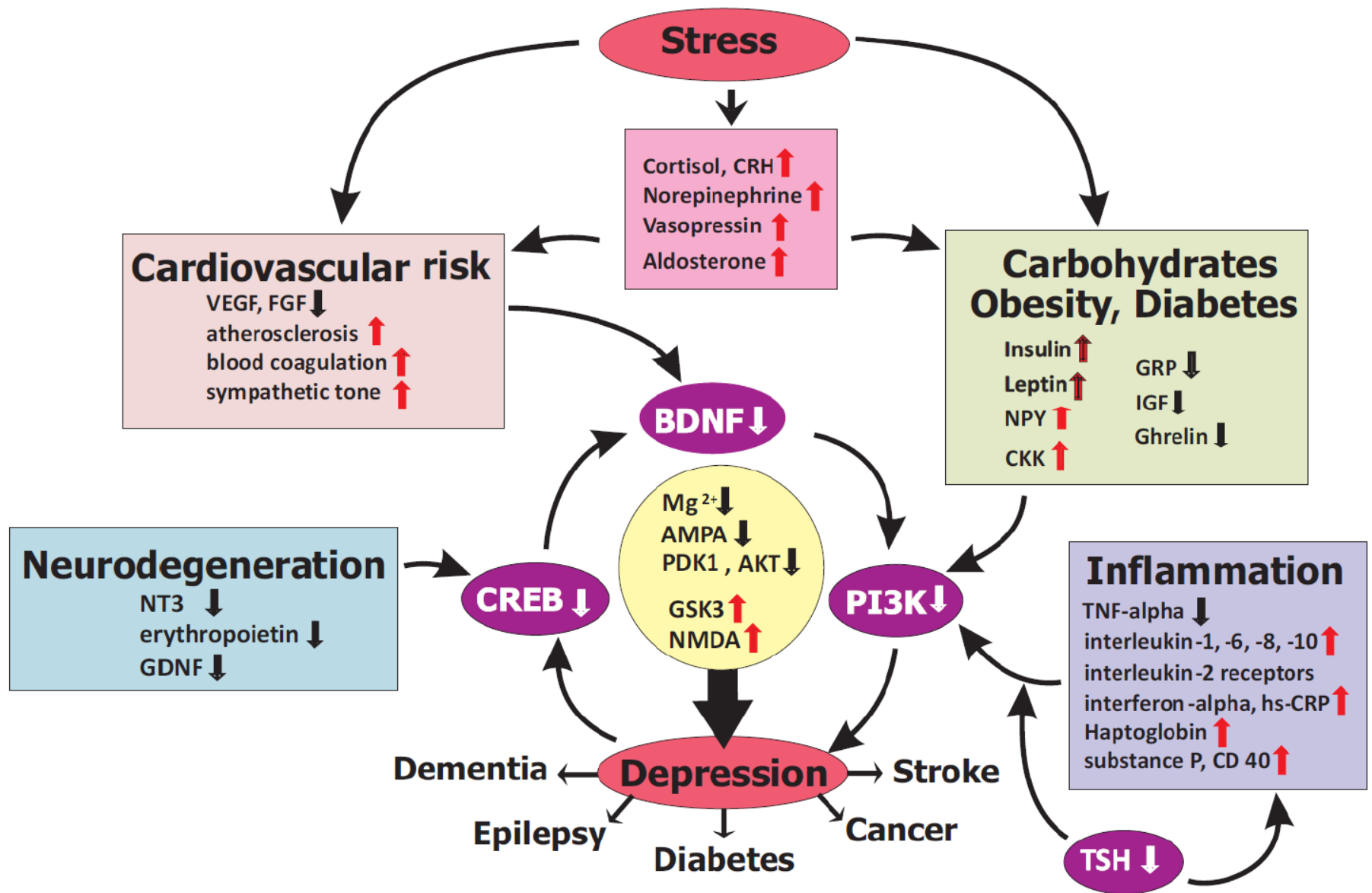


# Introduction to MDD

Abhi Saxena, M.D.



## Diagnostic Criteria

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

**Note:** Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

**Note:** Criteria A–C represent a major depressive episode.

**Note:** Responses to a significant loss (e.g., bereavement, financial ruin, losses from a

- D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
- E. There has never been a manic episode or a hypomanic episode.

**Note:** This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

*Specify:*

**With anxious distress**

**With mixed features**

**With melancholic features**

**With atypical features**

**With mood-congruent psychotic features**

**With mood-incongruent psychotic features**

**With catatonia. Coding note:** Use additional code 293.89 (F06.1).

**With peripartum onset**

**With seasonal pattern** (recurrent episode only)

Severity/course specifier	Single episode	Recurrent episode*
Mild	296.21 (F32.0)	296.31 (F33.0)
Moderate	296.22 (F32.1)	296.32 (F33.1)
Severe	296.23 (F32.2)	296.33 (F33.2)
With psychotic features**	296.24 (F32.3)	296.34 (F33.3)
In partial remission	296.25 (F32.4)	296.35 (F33.41)
In full remission	296.26 (F32.5)	296.36 (F33.42)
Unspecified	296.20 (F32.9)	296.30 (F33.9)

# Prevalence

- 12-month prevalence in U.S.: 7%
- Lifetime prevalence: 15%\*
- In 2000, 4<sup>th</sup> most common medical condition, by 2020 WHO estimates it will be 2<sup>nd</sup>
- \$86 Billion
- Females 1.5-3 fold higher rate than males
- Incidence at any age but peaks in 20s
- \* 25-30% for medical students

# Outcomes

- Worse outcomes associated with psychotic features, anxiety, personality disorders, severity of symptoms
- Chronicity likely points to other comorbidities
- Recovery begins within 3 months for 40% of individuals; within 12 months for 80%

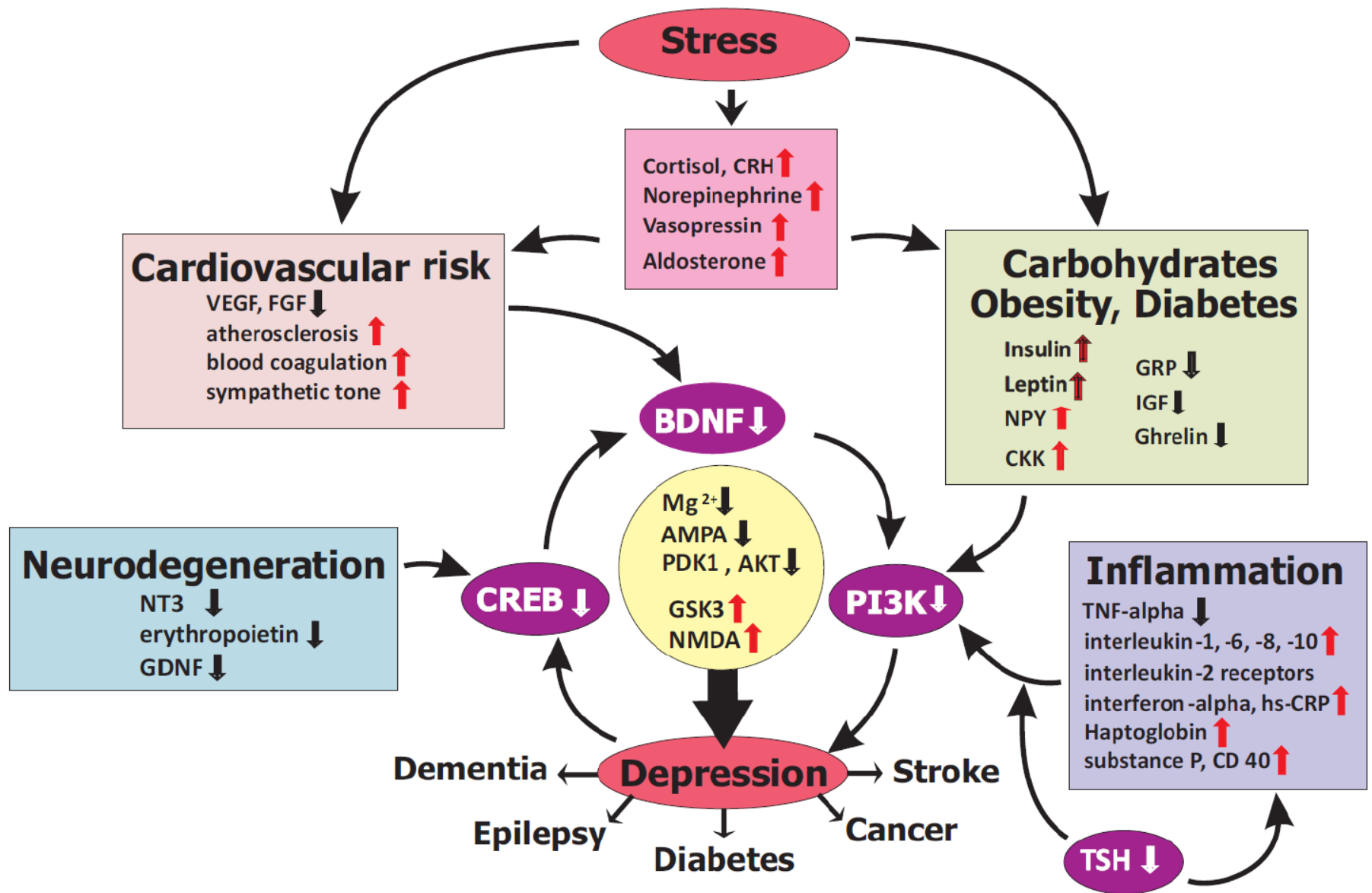
# Recurrence

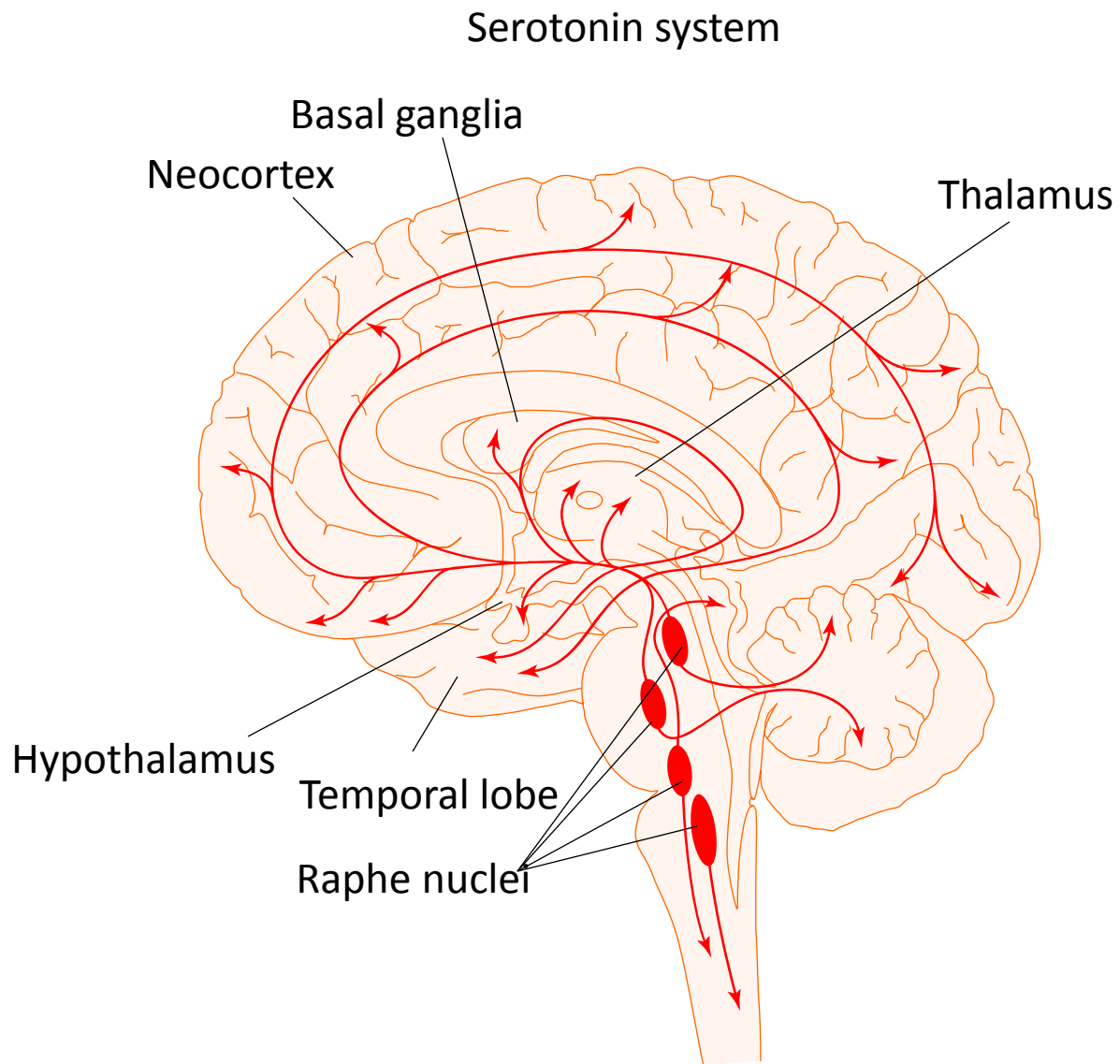
- As duration of remission (2 months w/ 0 symptoms or 1-2 mild symptoms only) increases, risk of recurrence decreases
- Risk of recurrence higher when: preceding episode was severe, individual is young, individual has experienced multiple episodes already
- Even mild depressive symptoms during remission is a strong predictor for recurrence



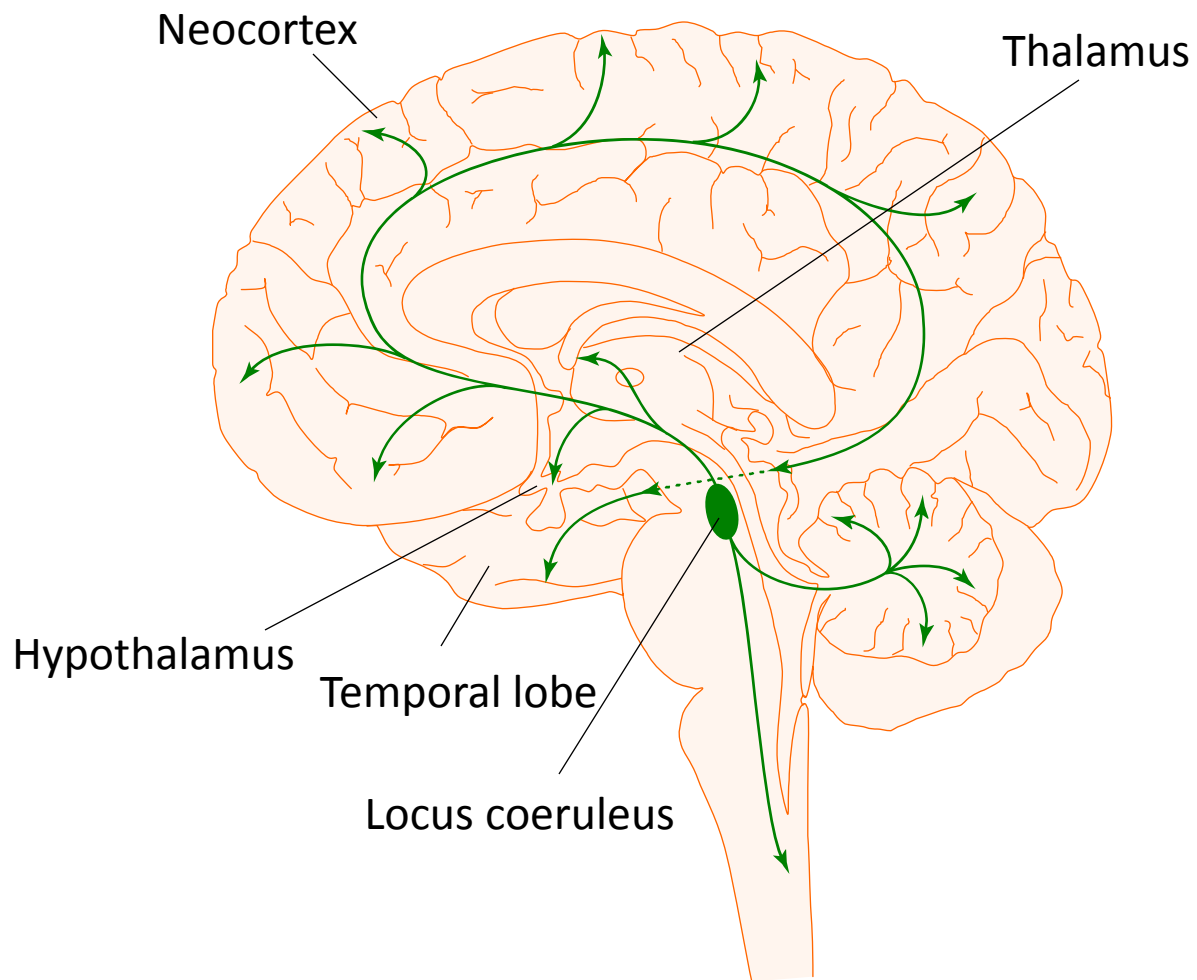
# Comorbidity

- substance-related disorders
- panic disorder
- obsessive-compulsive disorder
- anorexia nervosa
- bulimia nervosa
- borderline personality disorder

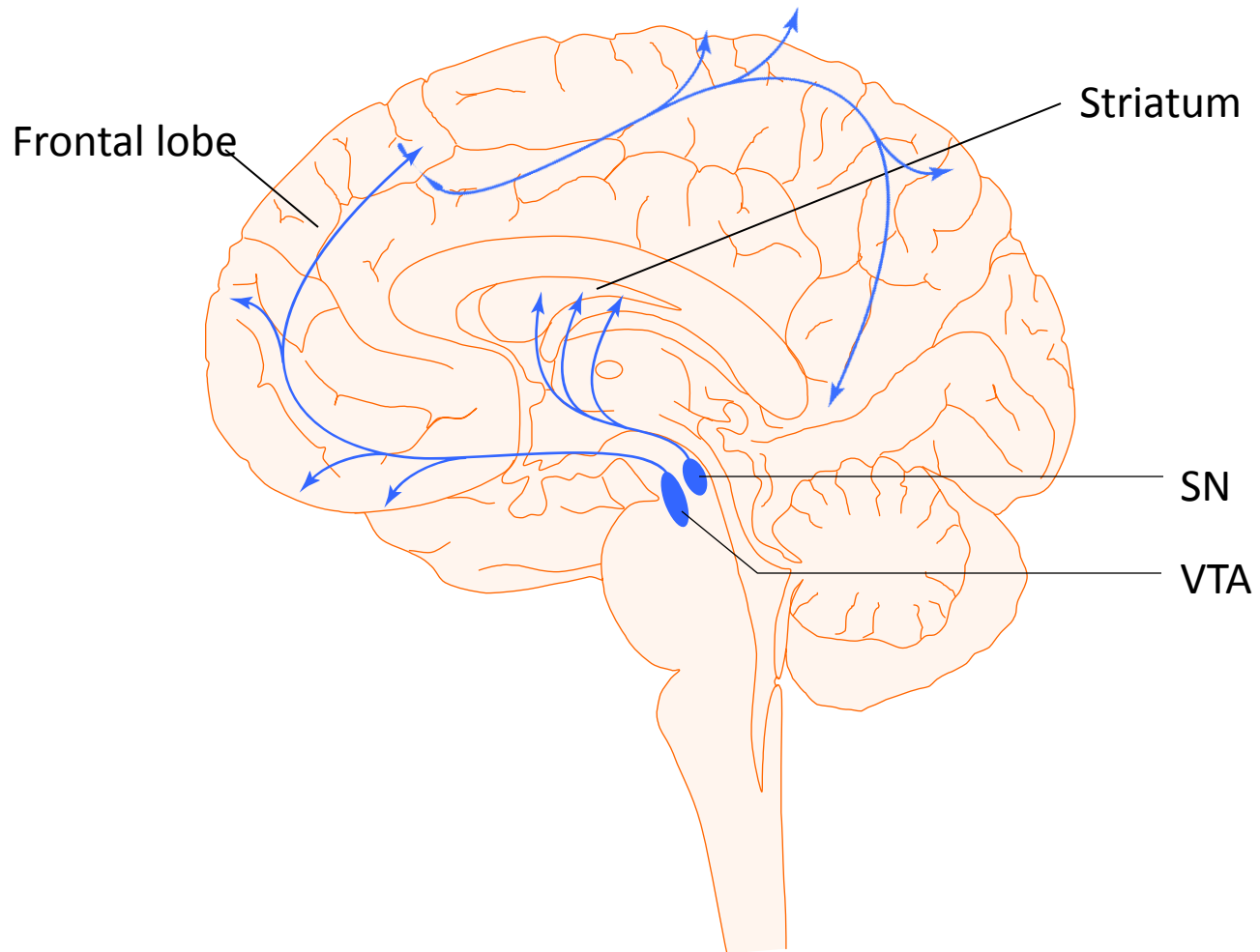




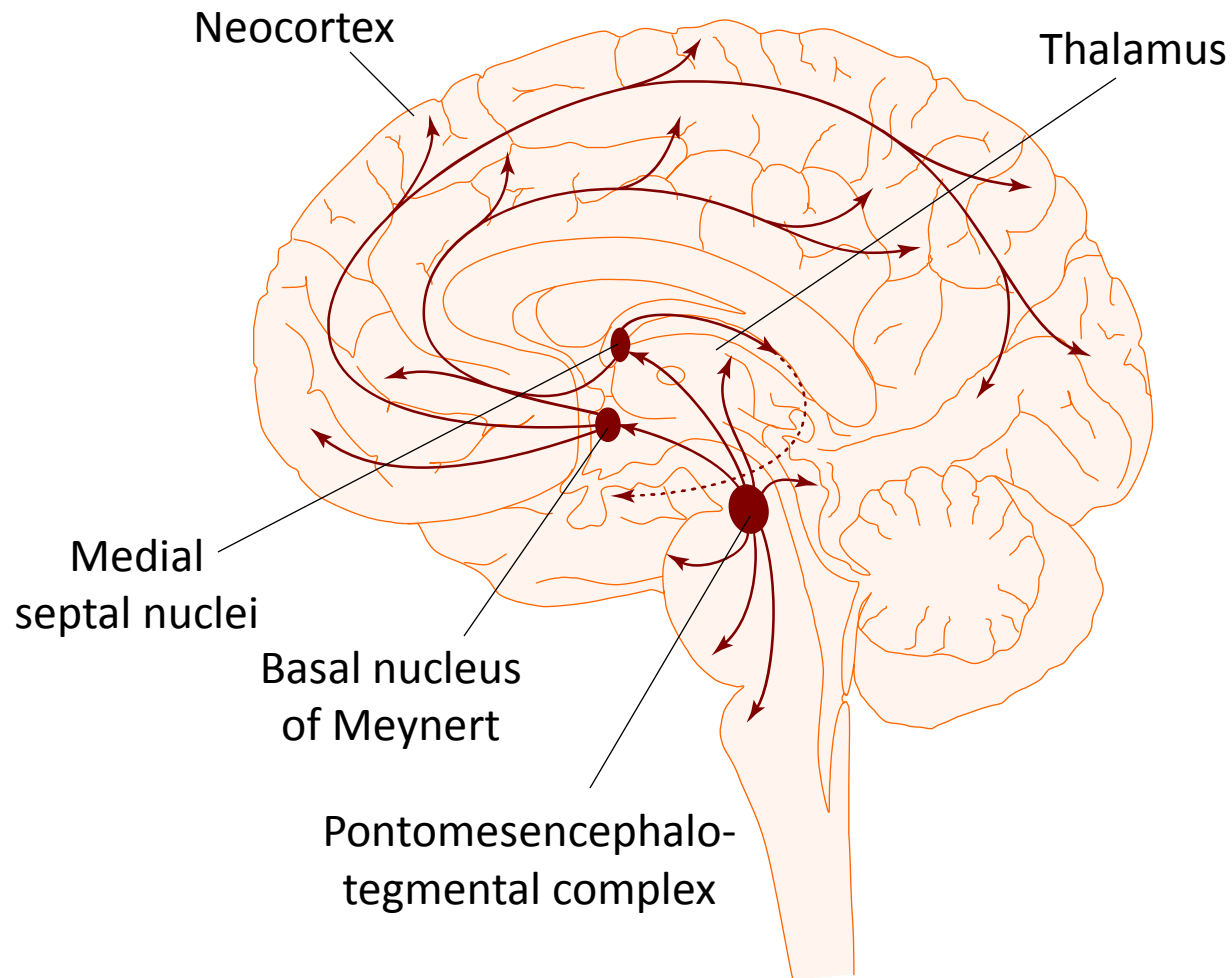
# Norepinephrine system



# Dopamine system

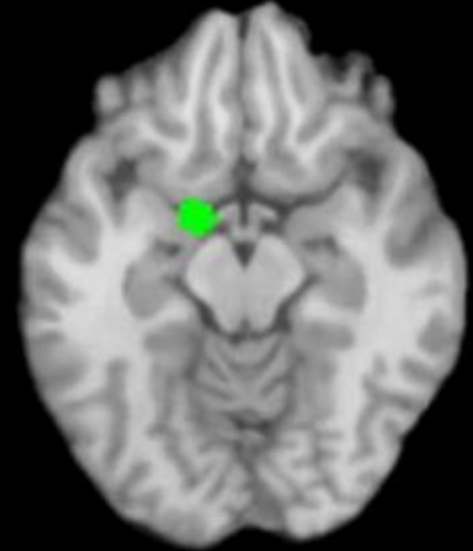
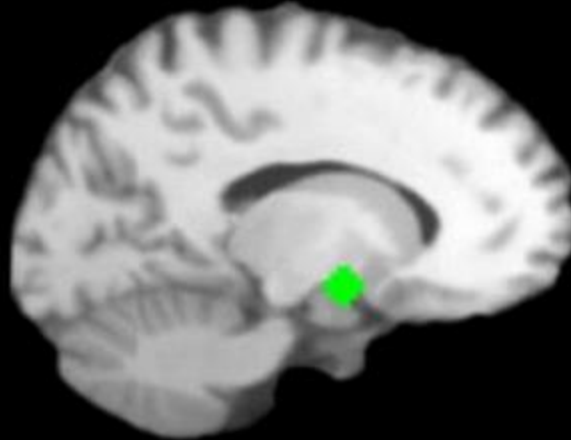
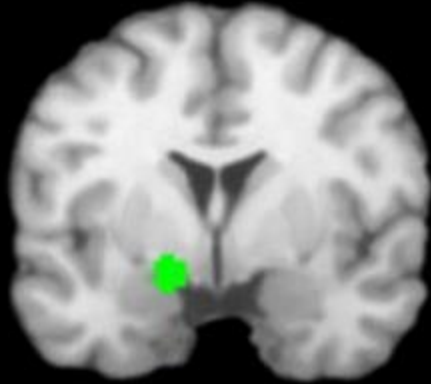


## Acetylcholine system

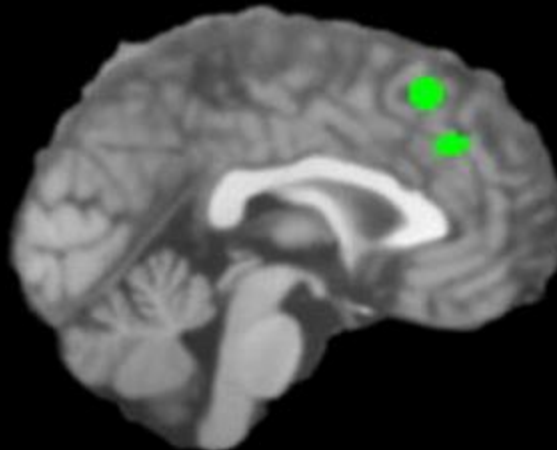
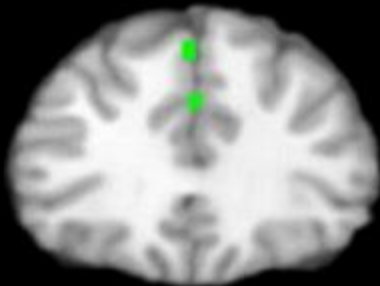


# Areas with decreased gray matter volume in depression

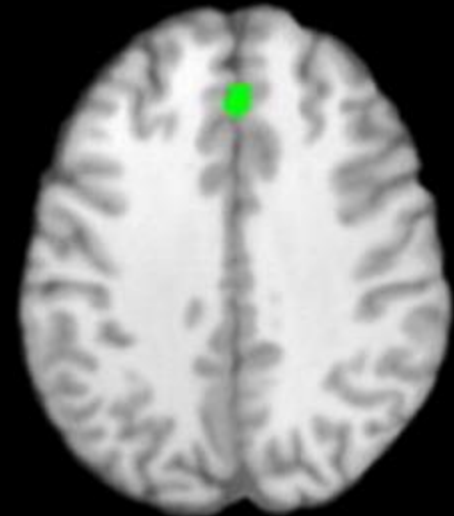
Left Amygdala



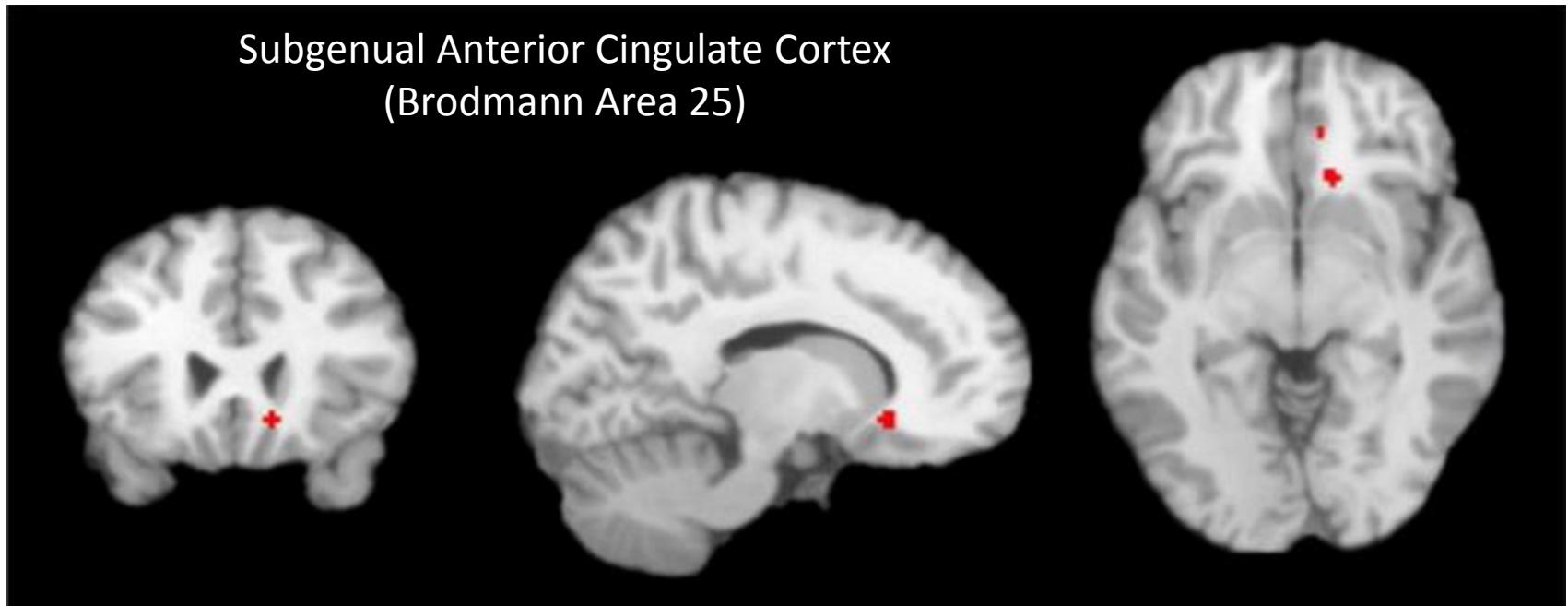
Left Dorsal Frontomedian Cortex



Paracingulate Cortex

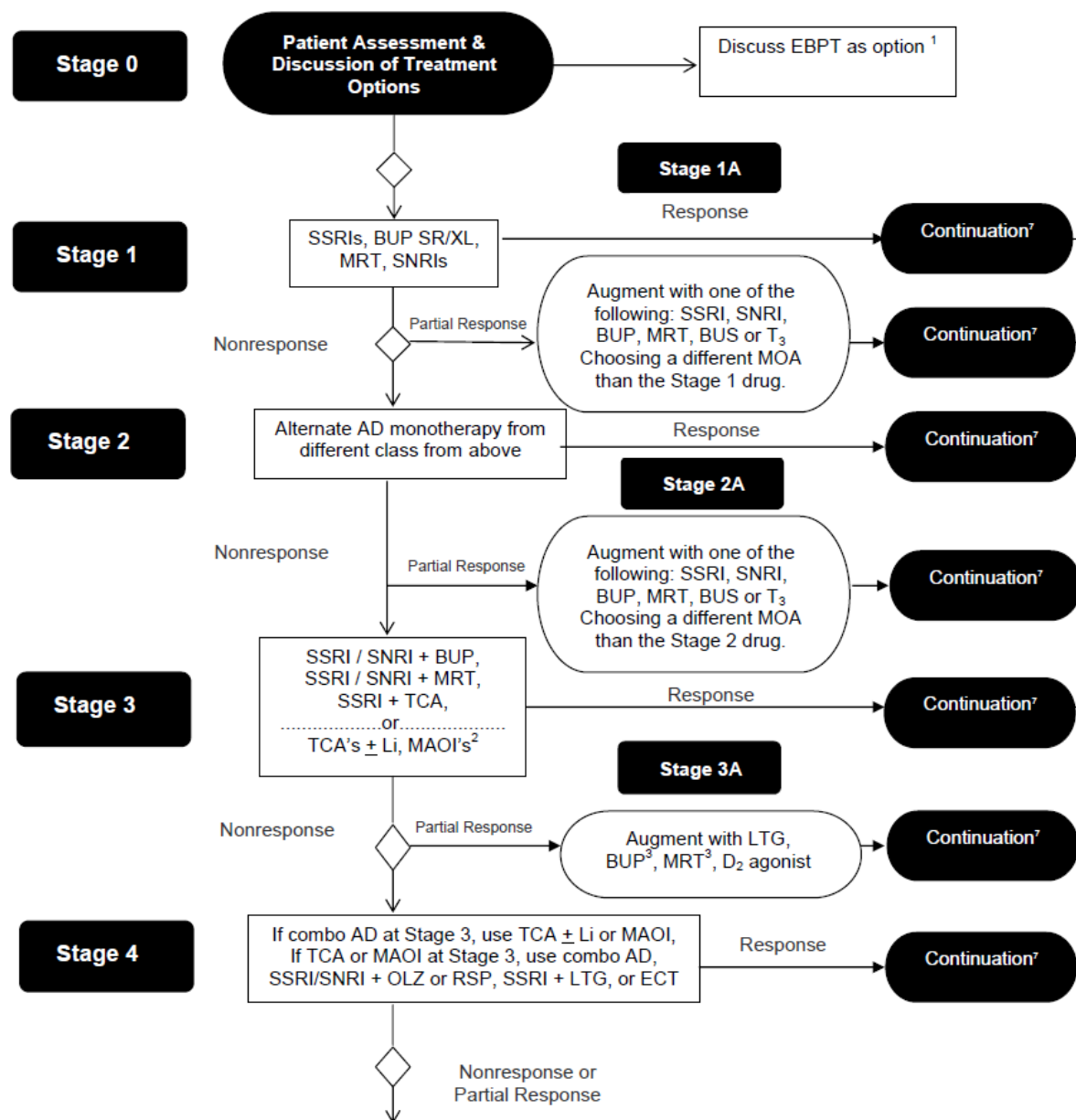


# Areas with increased resting metabolism in depression





## Algorithm for the Treatment of Major Depressive Disorder



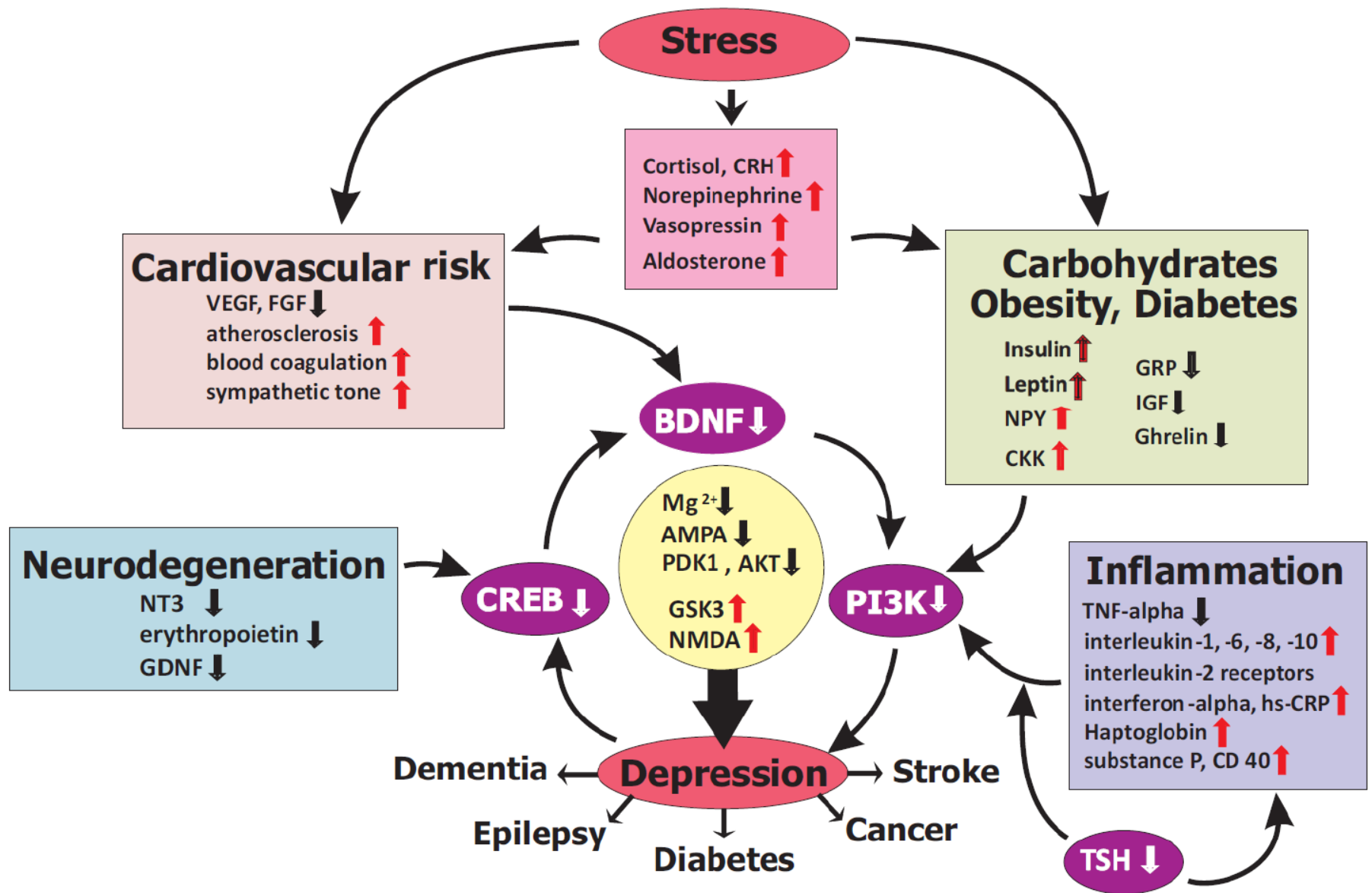
## Regulation of Hippocampal BDNF Expression

Factor	Treatment Duration	BDNF Expression
<b>STRESS</b>		
Immobilization	1, 7 days, (45 minutes/day)	↓
	45 minutes	
	8 hours	
Unpredictable	10 days, 4-15 weeks	↓
	19 days, 7-11 weeks	=
Footshock	60 minutes, (0,4 mA)	↓
Social isolation	6 hours	↓
Social defeat	10 minutes	↓
	5 weeks	↑
Maternal deprivation	24 hours, P9	↓
Swim stress	10 minutes/day, 14 days	↓
Restraint	4 hours/day, 3 days	↓
	6 hours/day, 21 days	=
		↓
	1 hour/day, 7 days	↑
<b>CORTICOSTERONE</b>	Acute, 7 days	↓
<b>ADRENALECTOMY</b>		↑

<b>ANTIDEPRESSANTS</b>		
<b>NRIs</b>		
Reboxetine	2-14 days	↑
Desipramine	14, 21 days	↑
	Acute, 14 days	=
Maprotiline	Acute, 14 days	=
<b>SSRIs</b>		
Fluoxetine	Acute, 14, 21 days	↑
	7 days	=
	4 days	↓
Paroxetine	Acute, 14 days	↑
Sertraline	Acute, 14, 21 days	↑
Citalopram	2, 9 days	↑
<b>SNRIs</b>		
<b>Dual</b>		
Venlafaxine	28, 35 days	↑
<b>Tricyclics</b>		
Imipramine	14, 20, 27 days	↑
	28 days	=
Amitriptyline	21 days	↑
<b>Atypical</b>		
Mianserine	21 days	↑
	Acute, 14 days	=
Tianeptine	21 days	=
<b>MORAGONISTS</b>		
Morphine, DAMGO <sup>1</sup>	Acute	↑

Curr Neuropharmacol. 2011 Dec;9(4):530-52. Neurotrophins role in depression neurobiology: a review of basic and clinical evidence. Neto FL, Borges G, Torres-Sanchez S, Mico JA, Berrocoso E.

<b>MAOI</b>		
Tranylcypromine	Acute, 2, 14-21 days	↑
	4, 14, 21 days	=
<b>Benzodiazepine</b>		
Olanzapine	35 days	↑
<b>Ketamine</b>	acute	↑
	acute, 7, 14 days	=
ECT	10, 21 days	↑
<b>Exercise</b>	1-28 days	↑
<b>Lithium</b>	1, 7 days	=
	14-28 days	↑



**Specific 5HT or NA reuptake inhibitors**  
(SSRIs eg. citalopram)  
(NRIs eg. reboxetine)  
Amplify 5HT or NA  
No anticholinergic effects

**Dual 5HT/NA reuptake inhibitors**  
(SNRIs eg. venlafaxine)  
Amplify 5HT + NA  
No anticholinergic effects

**Tricyclics**  
Amplify 5HT + NA  
Anticholinergic and other side effects

**'Atypical' antidepressants**

Free of major tricyclic side effects

Amplify 5HT and/or NA by a variety of mechanisms - e.g:

- Stimulation of 5HT<sub>1A</sub> receptors (buspirone)
- Disinhibition of NA/5HT by blockade of inhibitory receptors (eg. mirtazapine)

**MAOIs**

Amplify 5HT, NA, as well as DA and other amines  
Dietary side effects

**Selective MAO-A inhibitors**  
(eg. clorgyline)  
Amplify 5HT, NA  
Dietary side effects

**Reversible MAO-A inhibitors eg. moclobemide)**  
Amplify 5HT, NA  
No dietary side effects

# Psychotherapy for Major Depression

- Cognitive Behavioral Therapy (CBT)
- Interpersonal Therapy (IPT)
- Behavioral Activation Therapy
- Mindfulness Based Cognitive Therapy
- Less so: Family, couples, psychodynamic