

Understanding What Causes Schizophrenia: A Developmental Perspective

What causes schizophrenia? The short answer may be “nothing” or more precisely “no one thing.” In most cases, schizophrenia is an end result of a complex interaction between thousands of genes and multiple environmental risk factors -none of which on their own causes schizophrenia.

Twin studies and heritability of schizophrenia

Heritability estimates	%
Schizophrenia	80
Osteoarthritis of the hip	60
Hypertension	30-50

heritability is a statistical concept (represented as h^2) that describes how much of the variation in a given trait can be attributed to genetic variation.

Susceptibility genes in schizophrenia

The most likely mode of inheritance of schizophrenia is via multiple genes of small effect

Table 1

Gene	Chromosomal region	Gene function
NRG1	8p21–22	Axon guidance, synaptogenesis, glial differentiation, myelination, glutamatergic neurotransmission
DTNBP1	6p22.3	Presynaptic glutamate function
DISC1	t(1, 11) (q42; q14.3)	Neuronal migration, neurite architecture and intracellular transport
COMT	22q11	Dopamine metabolism
DAOA	13q22–34	Glutamatergic system

DTNBP1 = dysbindin; NRG1 = neuregulin 1; DAOA = D-amino acid oxidase activator; COMT = catecholamine-O-methyl transferase; DISC1 = disrupted in schizophrenia 1.

Vulnerabilità genetica

Geni di suscettibilità identificati: DISC1, NRG1, DTNBP1, COMT, DAOA

1. Fattori di rischio pre- e perinatali

Complicanze ostetriche

Infezioni virali

Stress e malnutrizione materna



Rendono l'individuo vulnerabile in quanto incidono sul neurosviluppo

2. Fattori di rischio in età infantile

Abuso infantile

Traumi cranici

Neglect



3. Fattori di rischio "tardivi"

Abuso di cannabis/sostanze

Migrazione

Urbanità

Avversità ambientale/eventi di vita



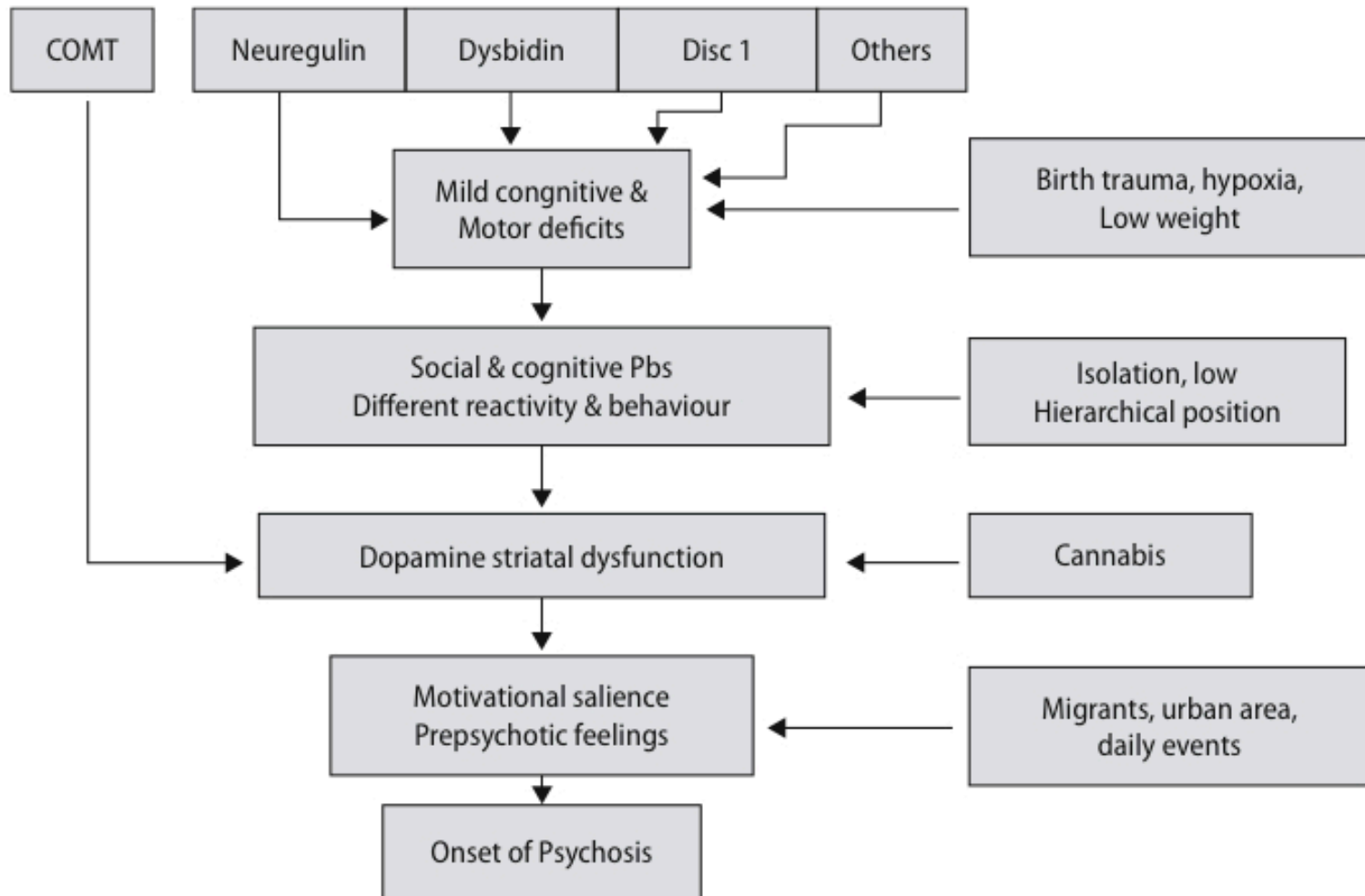
Interagiscono con i processi maturativi del cervello in età adolescenziale



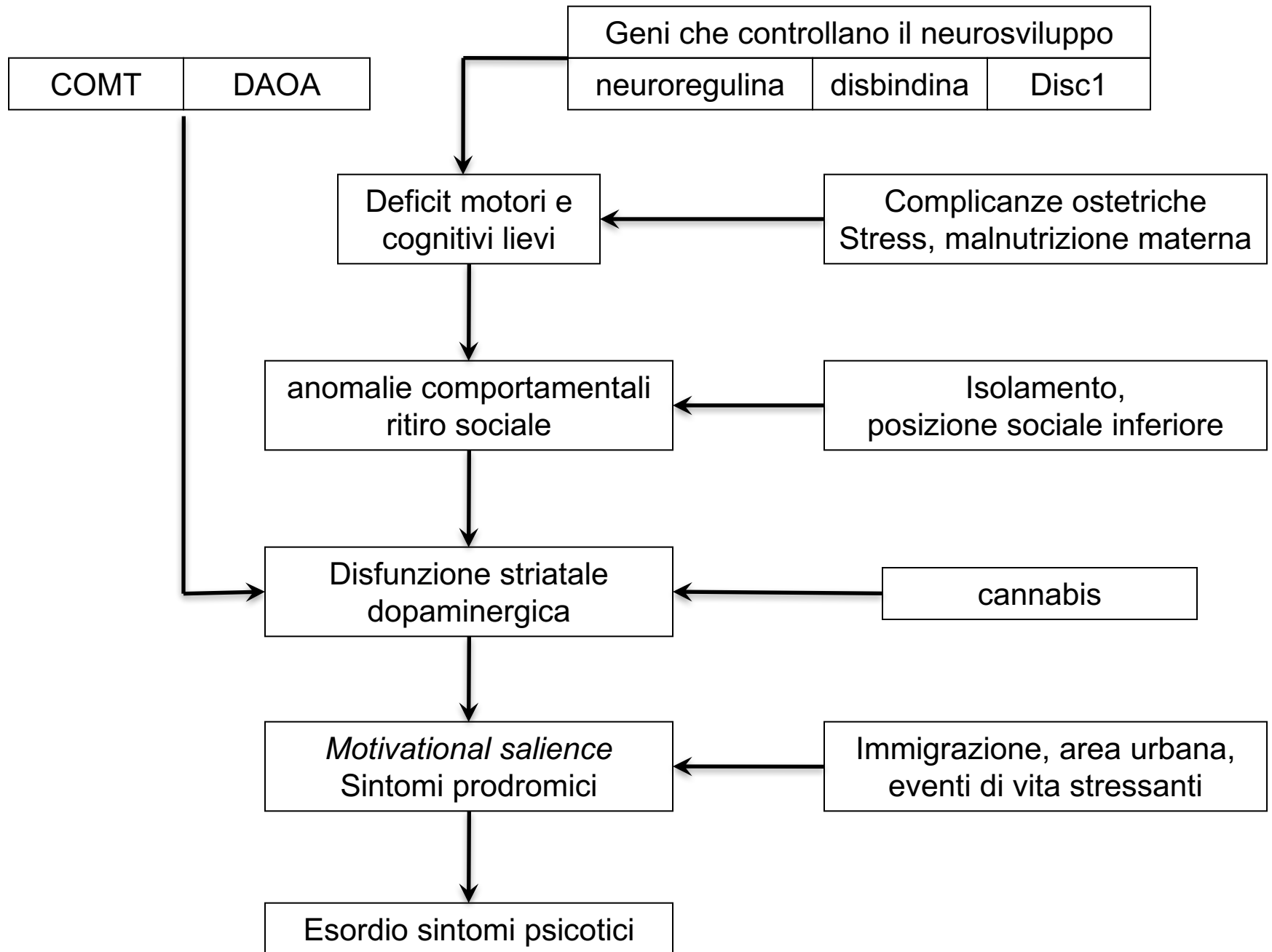
Esordio della schizofrenia

Interazione tra fattori di rischio genetici e ambientali
nel determinare l'esordio della schizofrenia

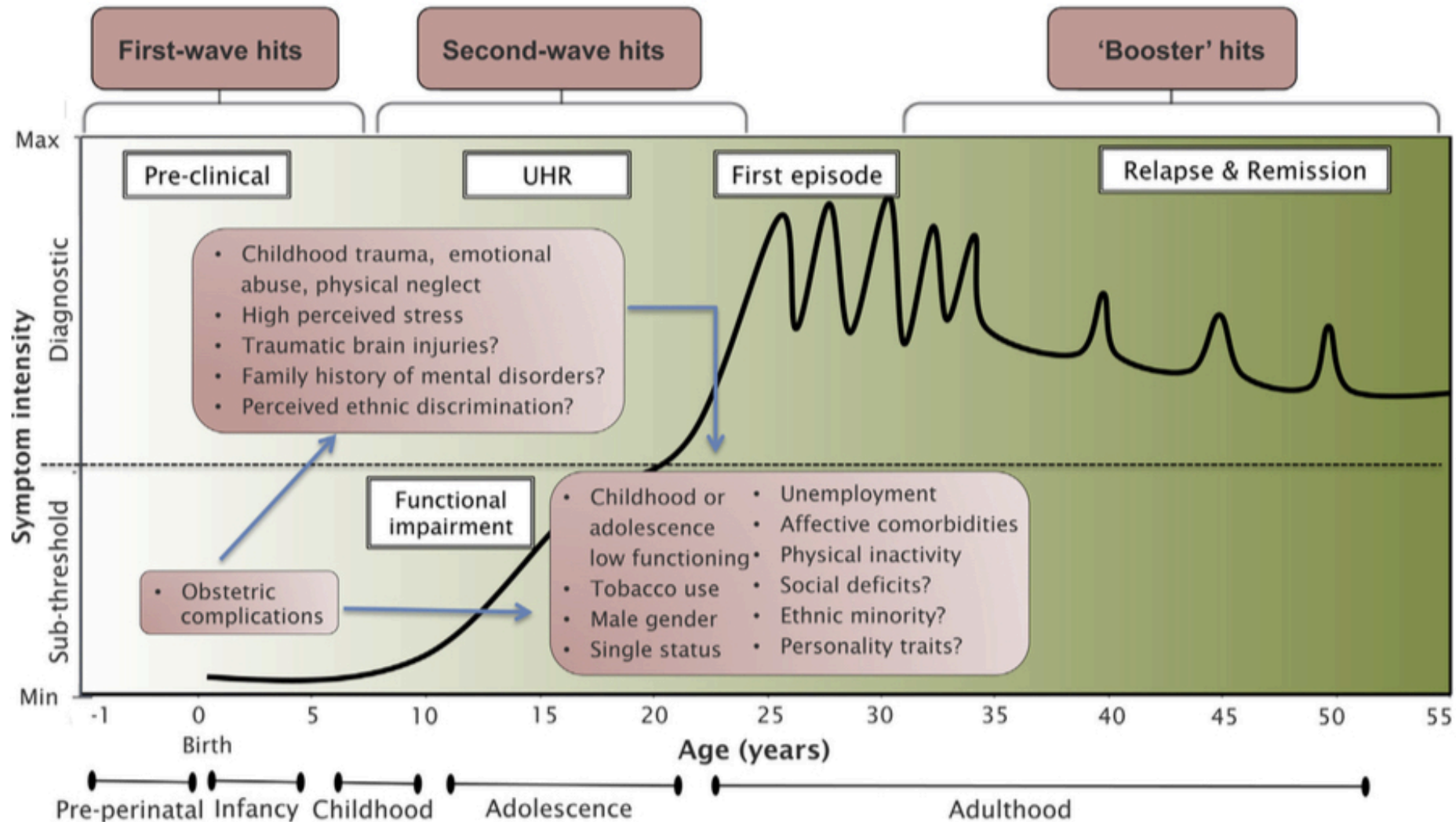
Schizophrenia: multiple genes of small effect and specific events at a certain period



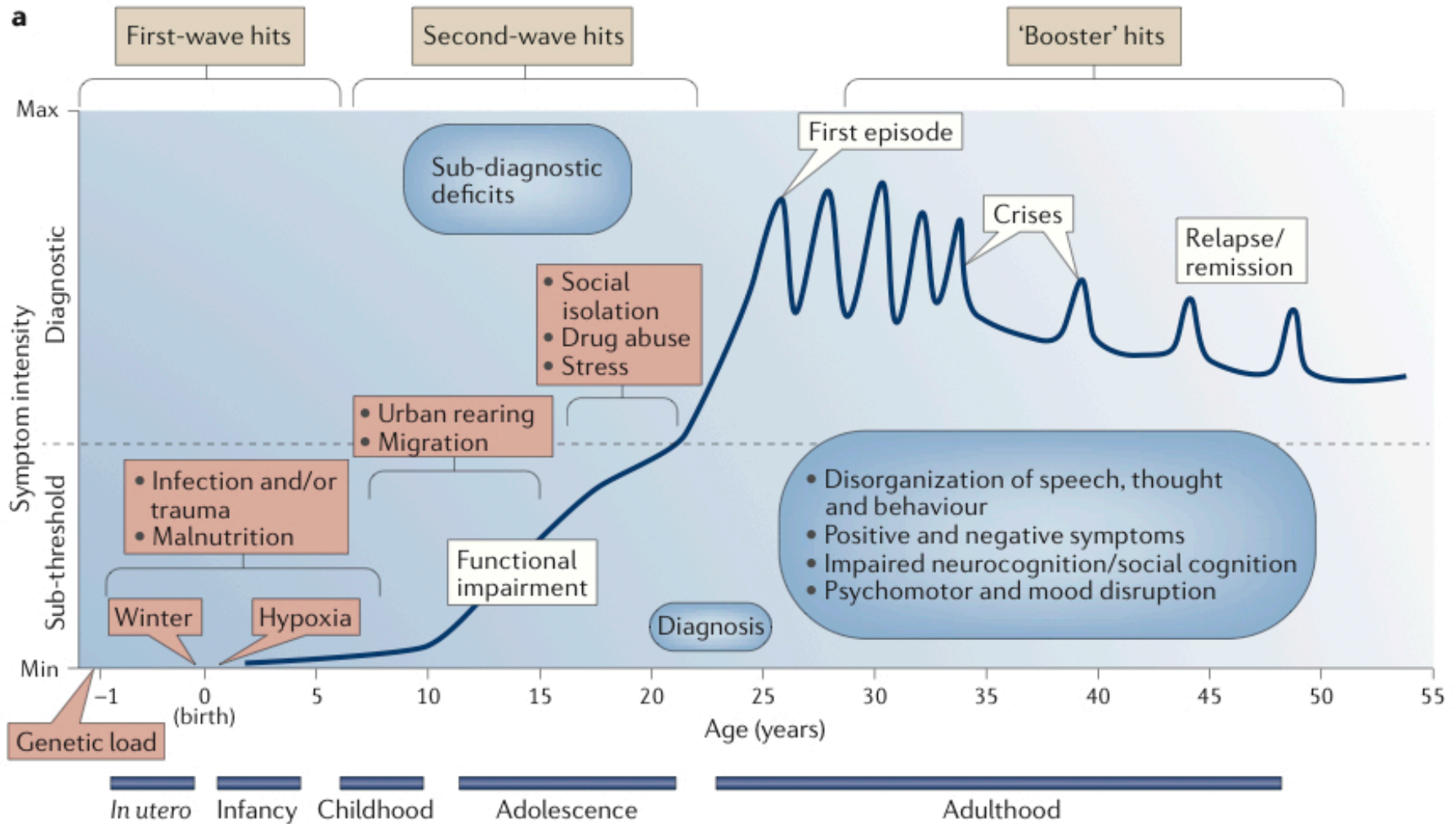
modello integrato per l'esordio dei sintomi psicotici



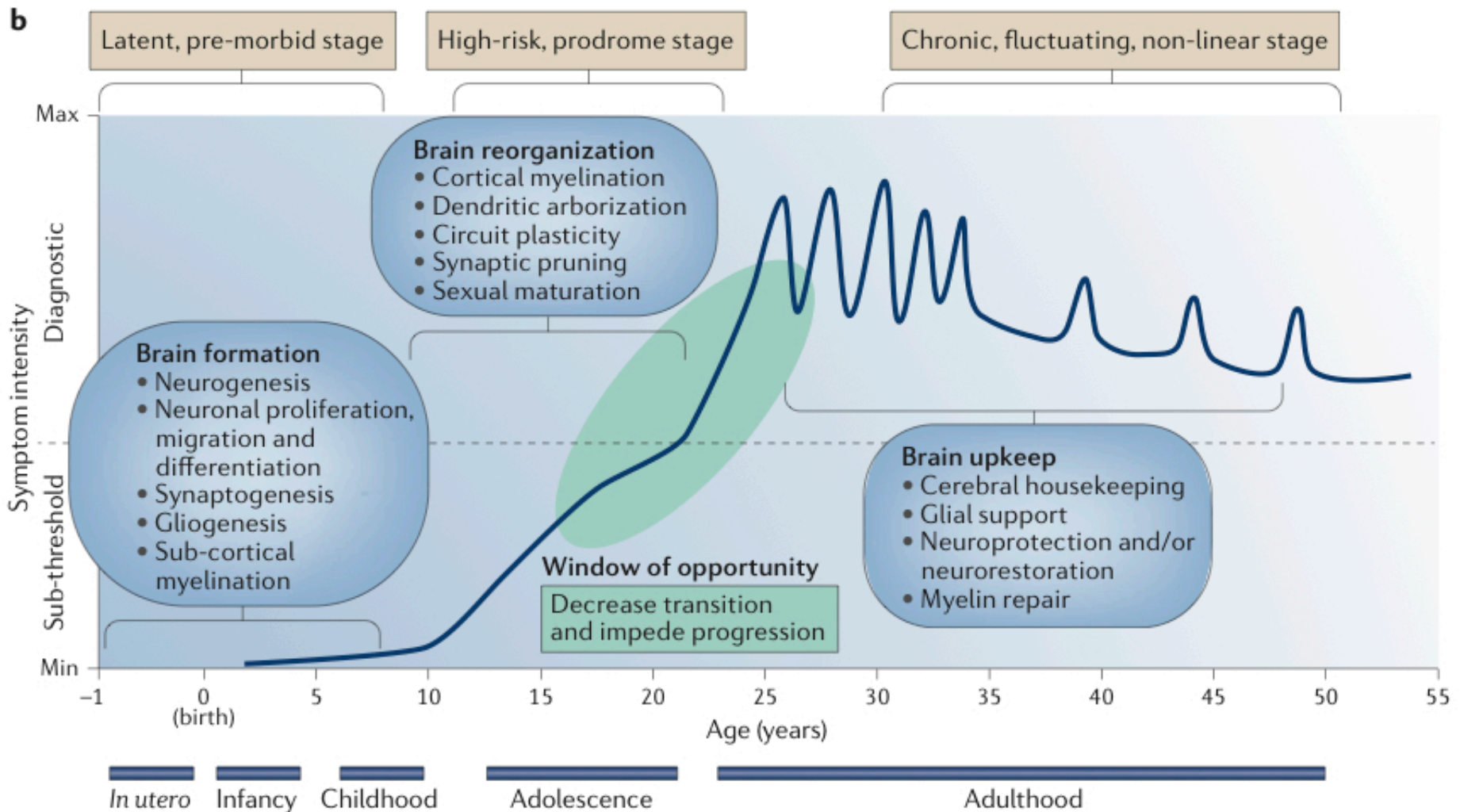
Deconstructing vulnerability for psychosis: Meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk



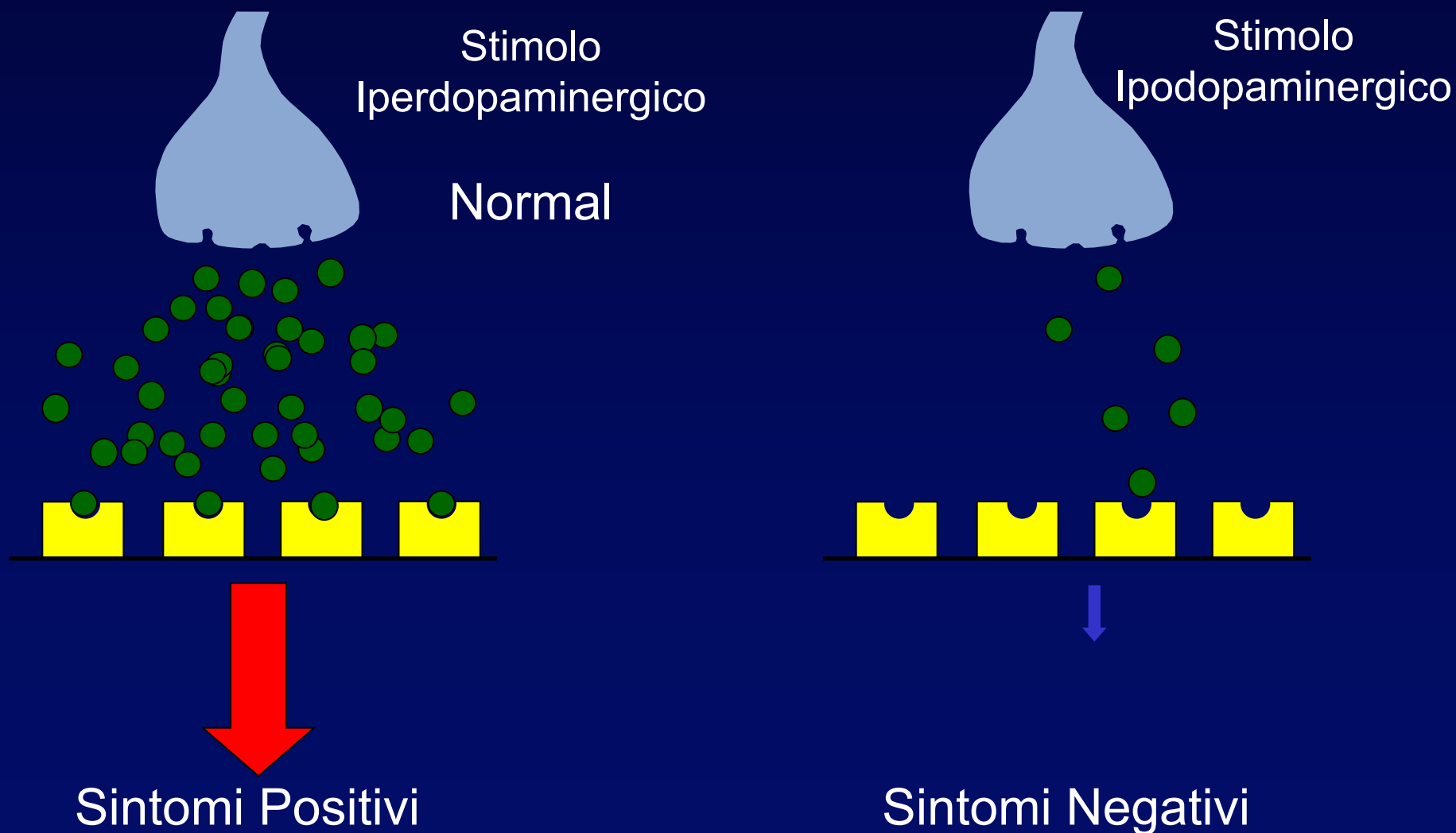
Onset and progression of schizophrenia in relation to risk factors



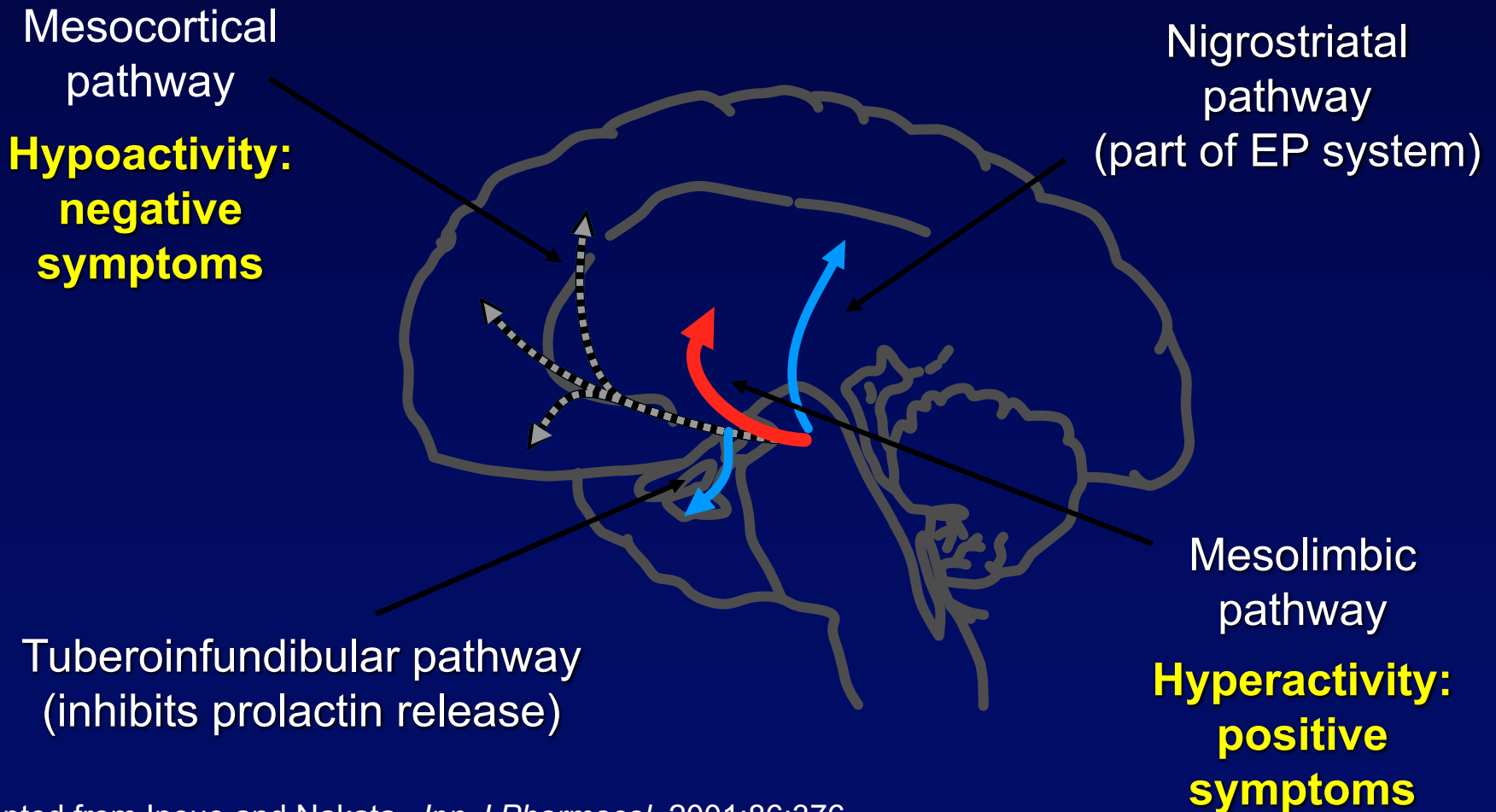
developmental processes affected by schizophrenia



Teoria Dopaminergica della Schizofrenia



Dopamine Hypothesis of Schizophrenia



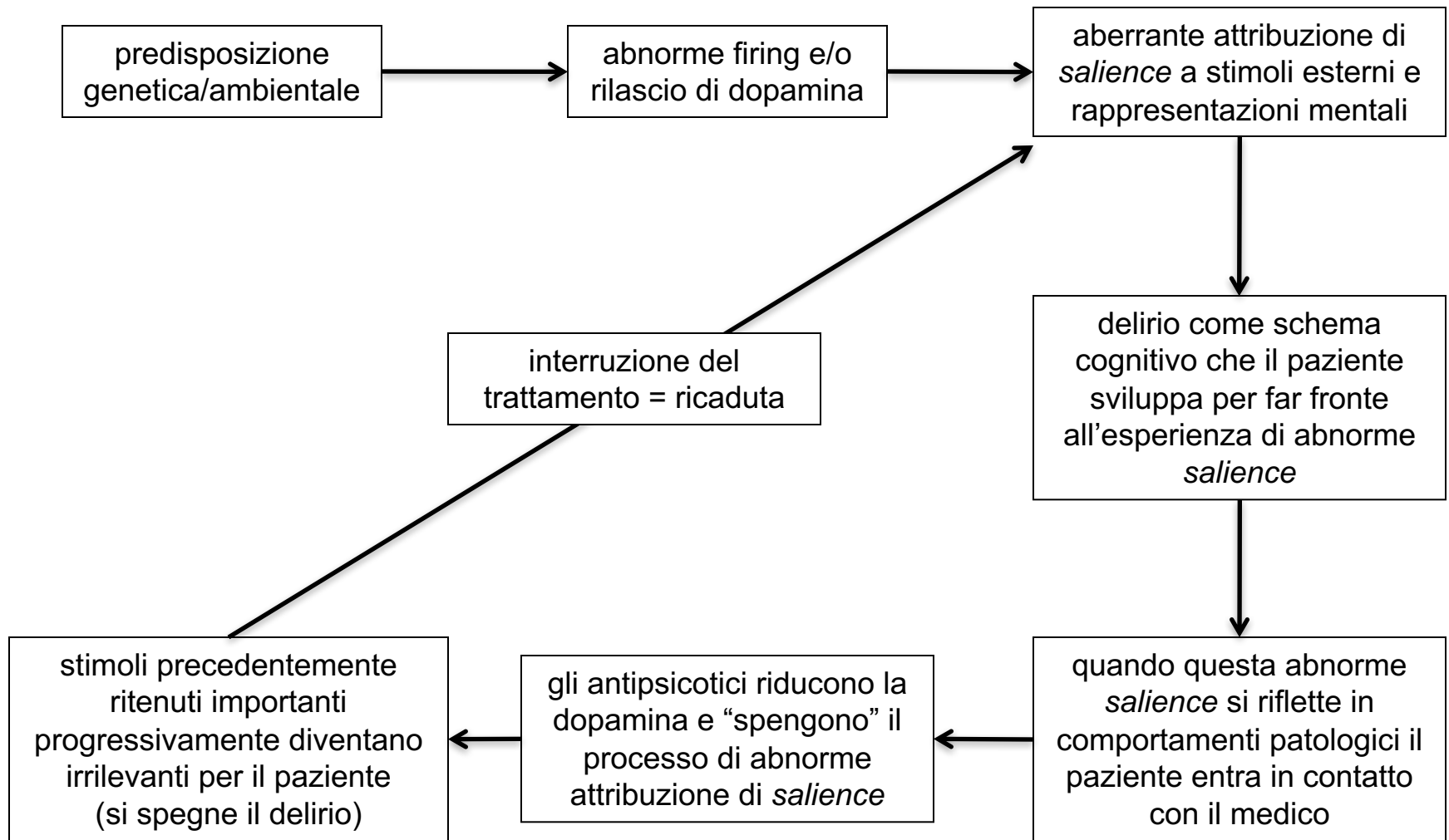
Pathophysiology of schizophrenia



Why a change in dopamine concentrations leads a person to become convinced that their colleagues are conspiring and the police is out to get them?

How dopaminergic abnormalities leads to the clinical expression of the disease?

descrizione dell'ipotesi di Kapur che lega la disfunzione dopaminergica alla sintomatologia positiva della schizofrenia



The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway

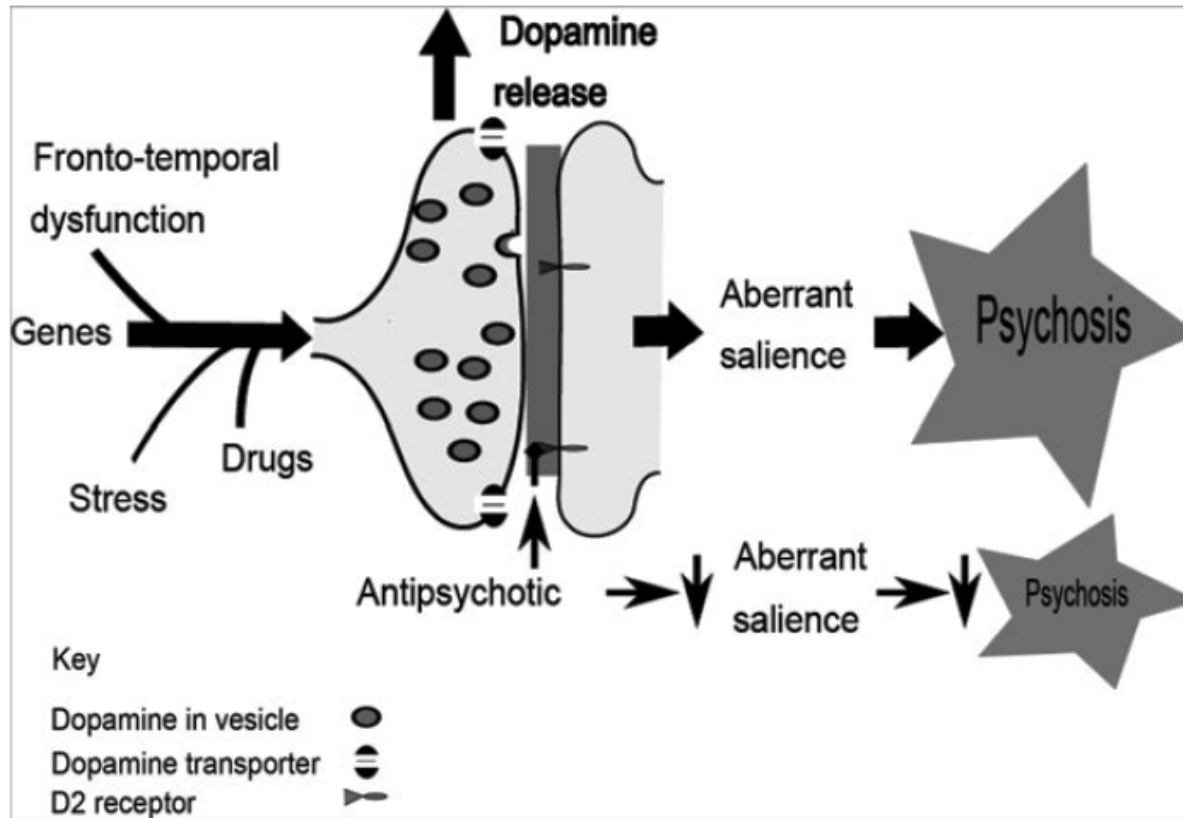


Fig. 1. Multiple hits interact to result in striatal dopamine dysregulation to alter the appraisal of stimuli and resulting in psychosis, whilst current antipsychotic drugs act downstream of the primary dopaminergic dysregulation.

The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway



Dopamine hypothesis of psychosis-in-schizophrenia

“..changes in multiple transmitter/neural systems underlie the cognitive dysfunction and negative symptoms of schizophrenia, and in many cases these dysfunctions precede the onset of psychosis.”

Schizophrenia: an integrated sociodevelopmental-cognitive model

Lancet 2014; 383: 1677–87

Oliver D Howes, Robin M Murray

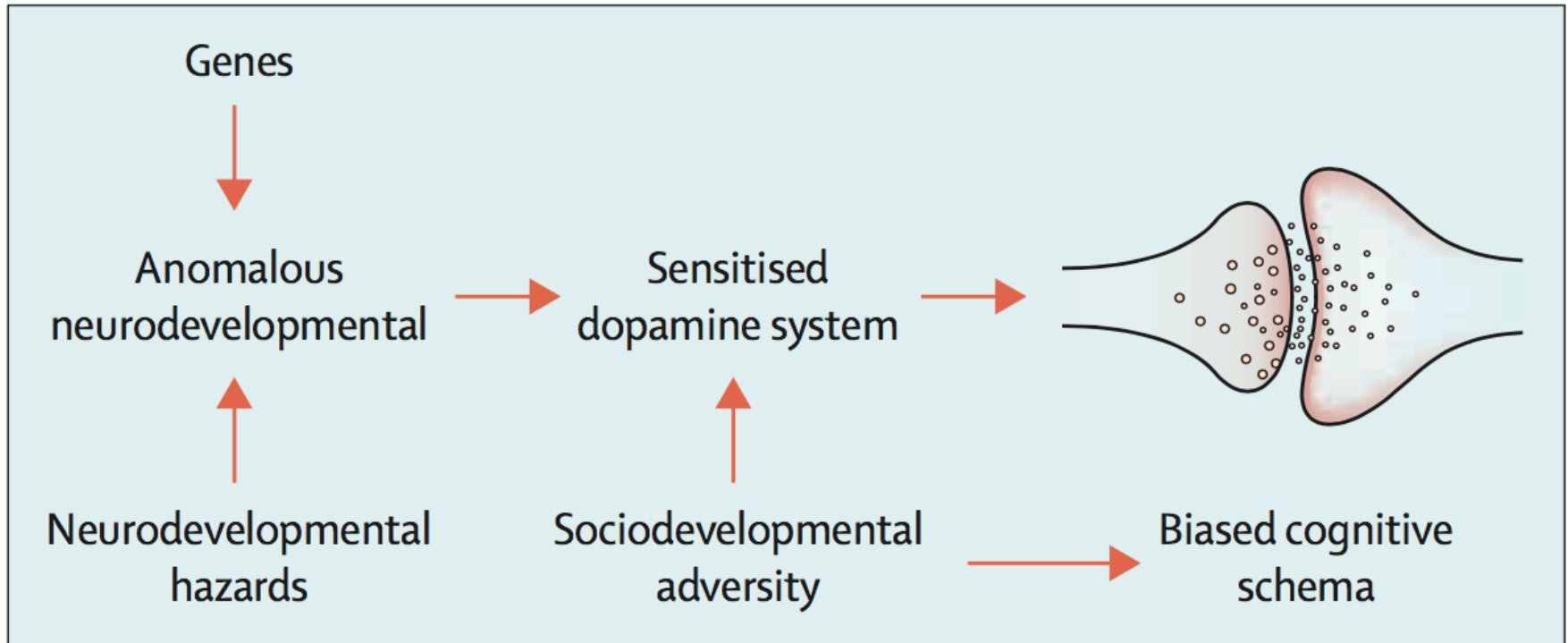


Figure 2: The effect of neurodevelopmental and sociodevelopmental risk factors for psychosis on the dopamine system and cognitive schema

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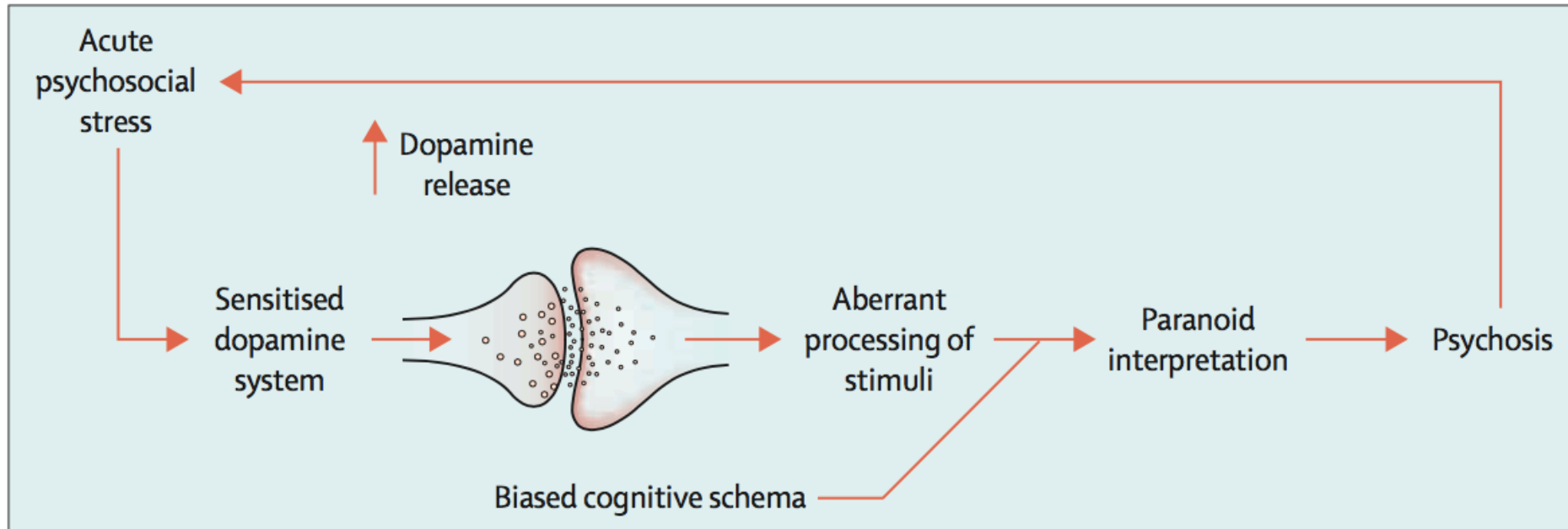


Figure 3: Model of the onset of psychosis showing the interaction between acute stress, dopamine dysfunction, and biased cognitive schema

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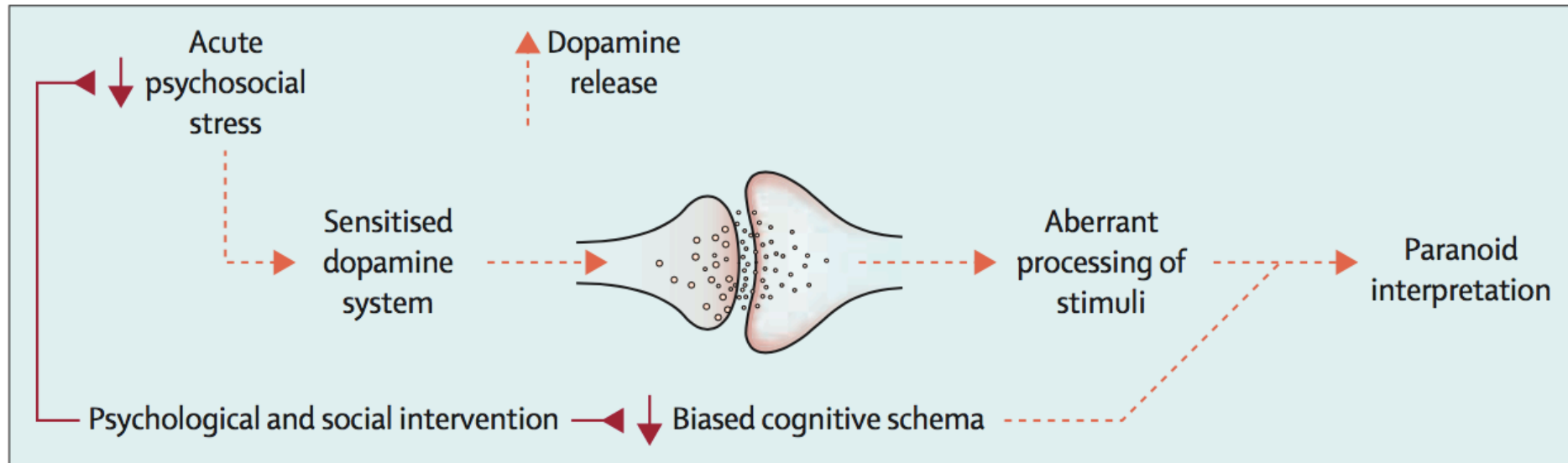


Figure 4: Sites at which psychosocial interventions could act to prevent psychosis

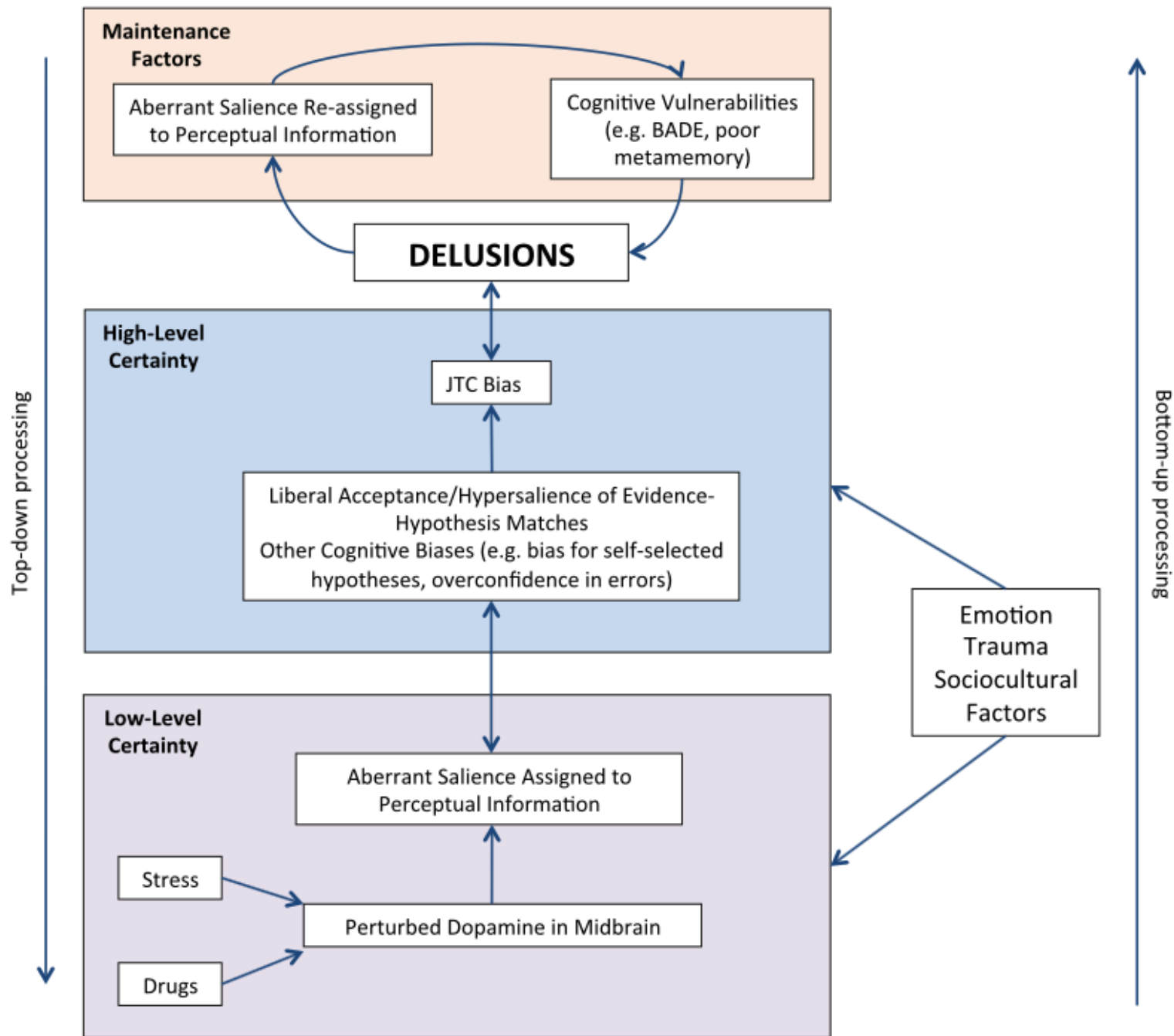


Fig. 1. Summary model of the formation and maintenance of delusional beliefs.

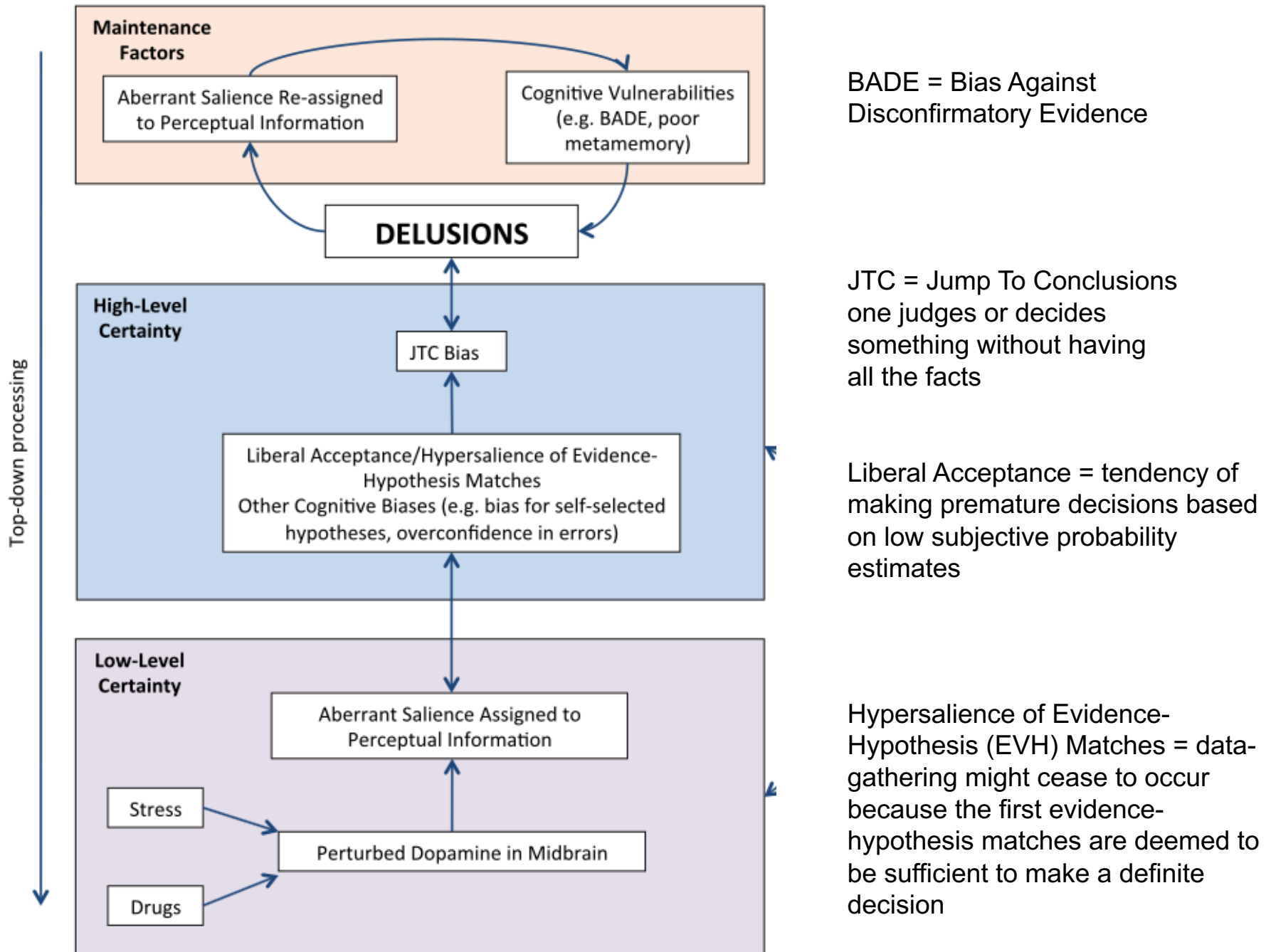


Fig. 1. Summary model of the formation and maintenance of delusions

I principali sottotipi clinici di schizofrenia e i sintomi più caratteristici.

	Sintomi positivi	sintomi disorganizzati	Sintomi negativi	Sintomi catatonici
Paranoide	++	+		
Disorganizzata	++	++	+	+
Catatonica		+	+	++
Residua		+	++	



Algoritmo per i sottotipi

CATATONICO



DISORGANIZZATO



PARANOIDE

Presenti sintomi catatonici, indifferentemente rispetto alla presenza di altri sintomi

Discorso e comportamenti disorganizzati, affettività appiattita o inadeguata
Ebefrenia di Kraepelin, Heckert

Se non catatonico o disorganizzato
Deliri e allucinazioni preminenti

RESIDUO

Sintomi residui, no sintomi di fase attiva

