091019 Skitsofreniaesitys -osa 1

Yl juha kemppinen

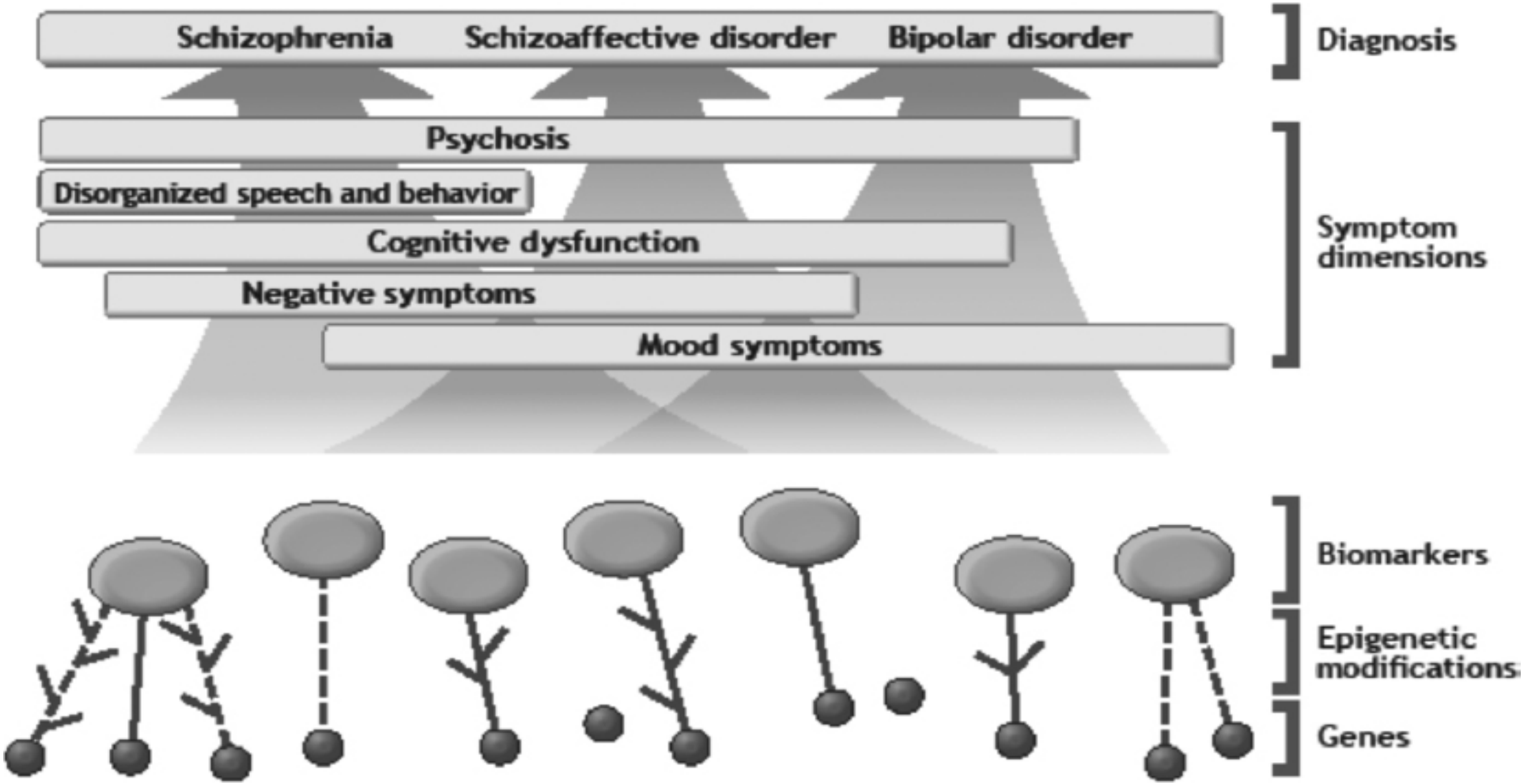
091019 Skitsofreniaesitys

- Agenda

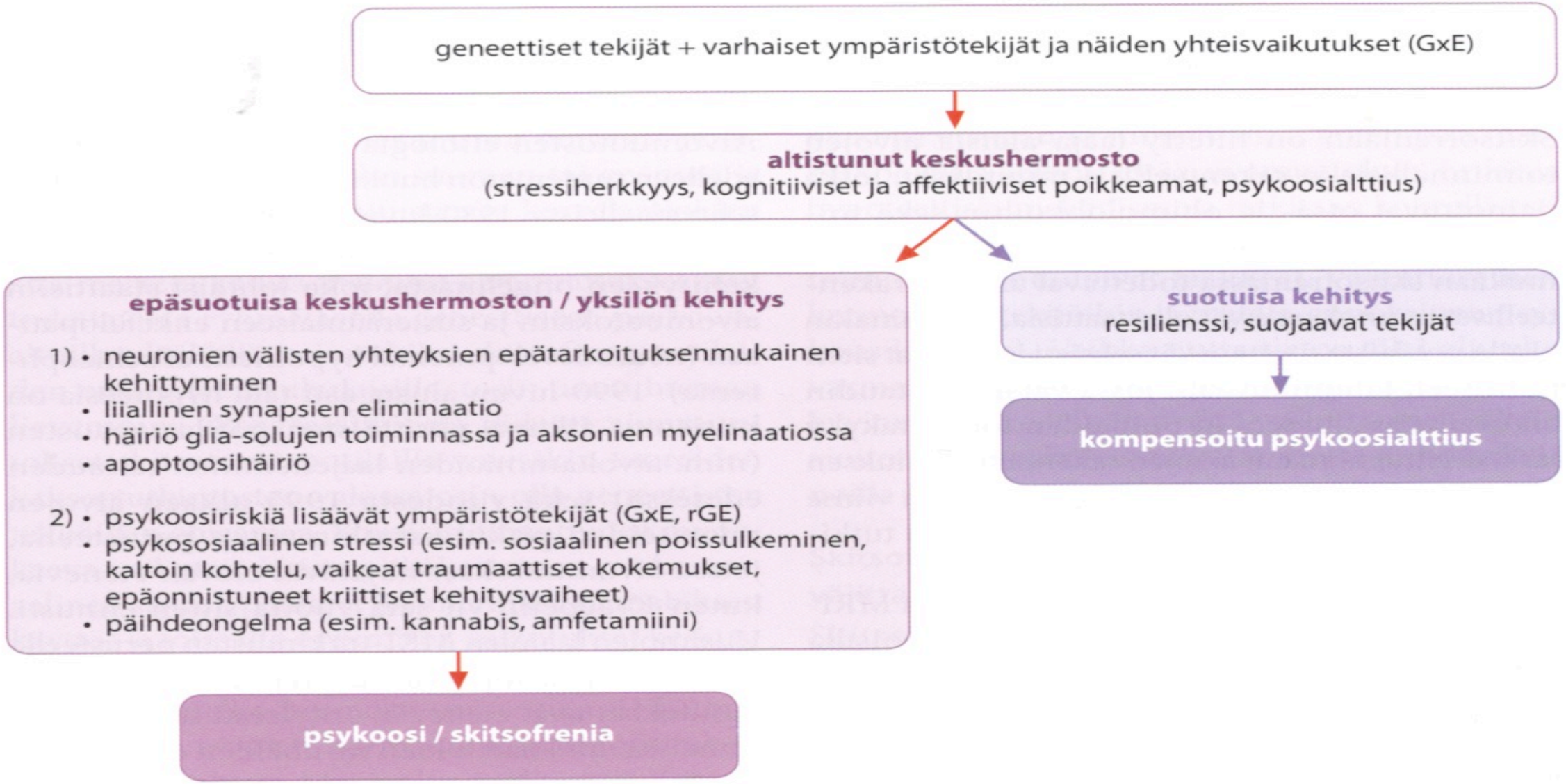
1) Skitsofrenia on hämmentävä kokonaisuus, yksi tauti?
2) Skitsofrenian epidemiologiaa
3) Skitsofrenian etiologia (neurobiologia)
4) Skitsofrenian diagnosointi
5) Skitsofrenian hoito
6) Muuta

091019 Skitsofreniaesitys

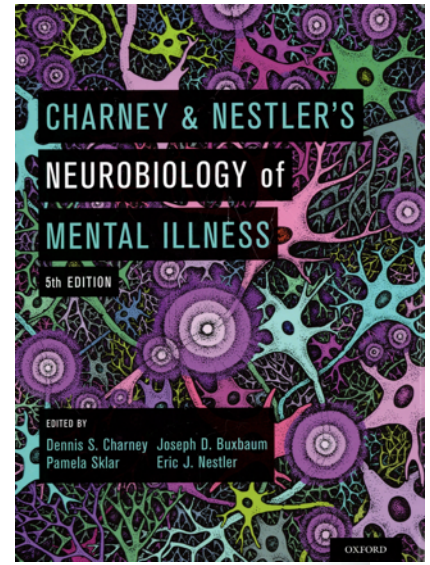
- **CAROL A. TAMMINGA, M.D. (Kaplan&Sadocks, 2017, 10th ed)**
- Schizophrenia is arguably one of the most puzzling yet disabling of all brain diseases,
  - with its severe and persistent psychotic manifestations accompanied by
  - variable cognitive dysfunction and
  - profound psychosocial impairment.



Kaplan&Sadock´s, 2017,10th ed



Kuva 2. Skitsofrenian puhkeamiseen vaikuttavia tekijöitä stressi-haavoittuvuusmallista mukailtuna.



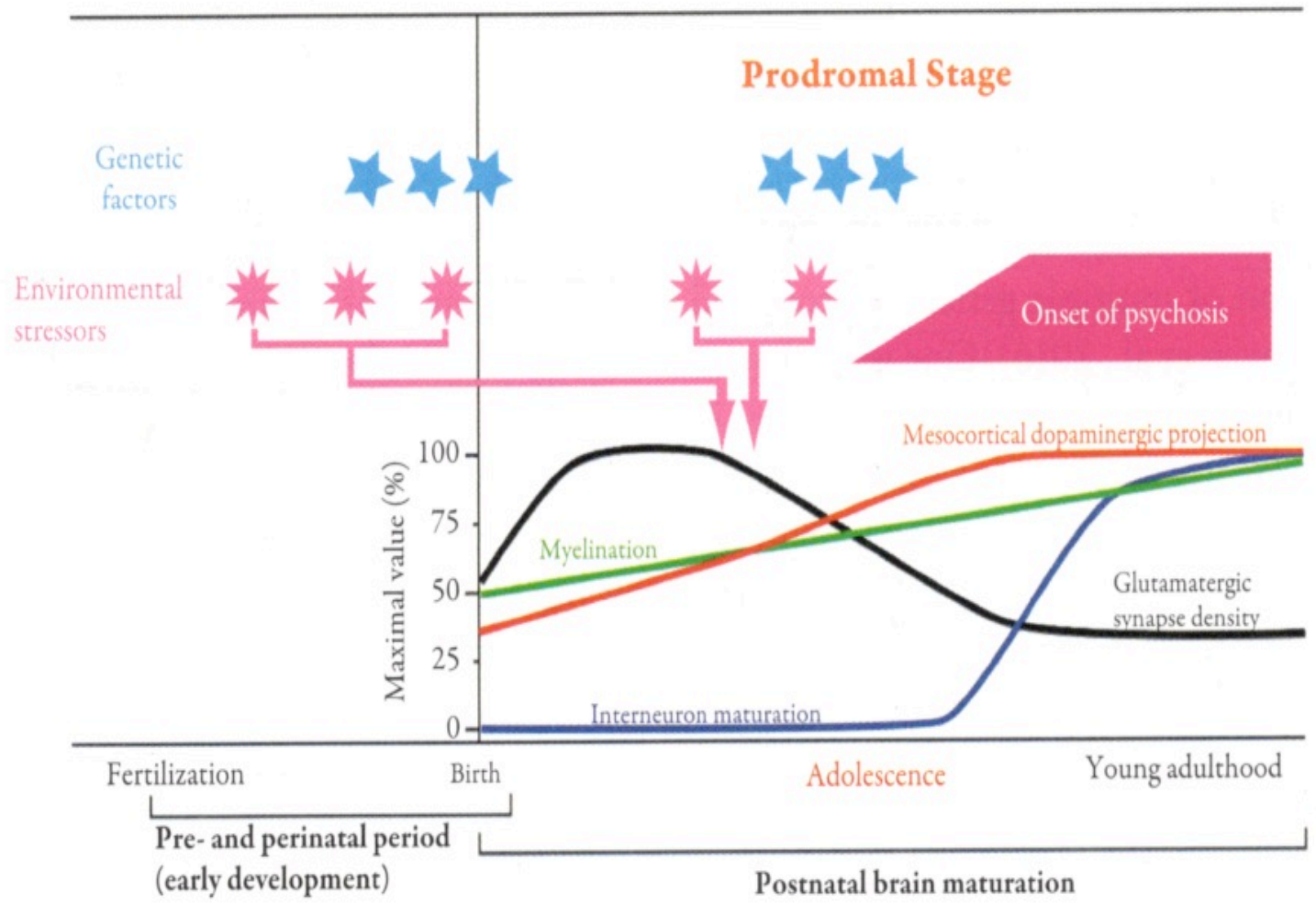
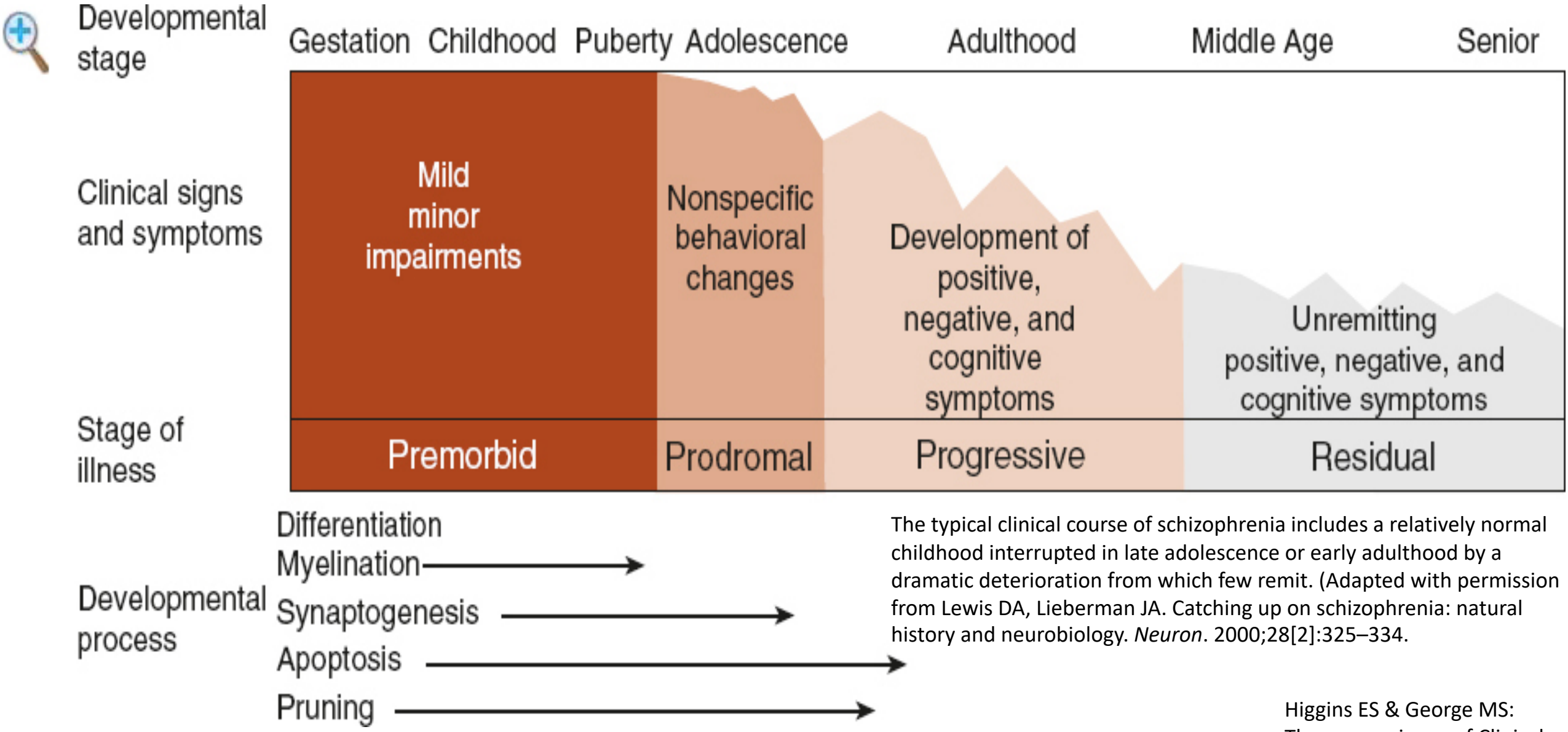


Figure 19.1 Genetic and environmental risk factors that occur over the neurodevelopmental trajectory may impair crucial developmental processes, accumulating to manifest as abnormal brain maturation and psychotic symptoms in early adulthood. Figure adapted with permission from Jaaro-Peled et al. (2009).



The typical clinical course of schizophrenia includes a relatively normal childhood interrupted in late adolescence or early adulthood by a dramatic deterioration from which few remit. (Adapted with permission from Lewis DA, Lieberman JA. Catching up on schizophrenia: natural history and neurobiology. *Neuron*. 2000;28[2]:325–334.

Higgins ES & George MS:
The neuroscience of Clinical Psychiatry, 2019, 3rd ed

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Table 3–1. Ultra-high-risk criteria for psychosis

1. Must be age 15–25 years.
2. Must have been referred to a specialized service for help.
3. Must meet the criteria for one or more of the following three groups:

Group 1: attenuated positive psychotic symptoms	• Presence of at least one of the following symptoms: ideas of reference, odd beliefs or magical thinking, perceptual disturbance, paranoid ideation, odd thinking and speech, odd behavior and appearance • Frequency of symptoms: at least several times a week • Recency of symptoms: present within the last year • Duration of symptoms: present for at least 1 week and no longer than 5 years
Group 2: brief, limited, intermittent psychotic symptoms	• Transient psychotic symptoms; presence of at least one of the following symptoms: ideas of reference, magical thinking, perceptual disturbance, paranoid ideation, odd thinking or speech • Duration of episode: less than 1 week • Frequency of symptoms: at least several times per week • Symptoms resolve spontaneously • Recency of symptoms: must have occurred within the last year

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Group 3: trait and state risk factors	• Schizotypal personality disorder in the identified individual, or a first-degree relative with a psychotic disorder • Significant decline in mental state or functioning, maintained for at least 1 month and not longer than 5 years • Recency of symptoms: decline in functioning must have occurred within the past year

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Table 3–2. Advantages of prepsychotic intervention

- Onset of frank psychosis may be delayed, ameliorated, or prevented.
- Prodromal individuals may engage more quickly with treatment compared with patients who present late when psychotic symptoms are entrenched, social networks are more disrupted, and functioning is further deteriorated.
- Prodromal individuals may be more likely to accept treatment if full-blown psychosis does emerge compared with patients who have been unwell for longer before assistance is sought.
- A therapeutic relationship is already established with a treating team if frank psychosis develops.
- Effective treatment can be provided rapidly if the person does develop psychosis, possibly avoiding the need for hospitalization and minimizing the deleterious effect of extended untreated psychosis.
- Prepsychotic intervention offers the chance to research the onset phase of psychotic illness, which may provide insight into the core features of the psychopathology and psychobiology of psychosis.

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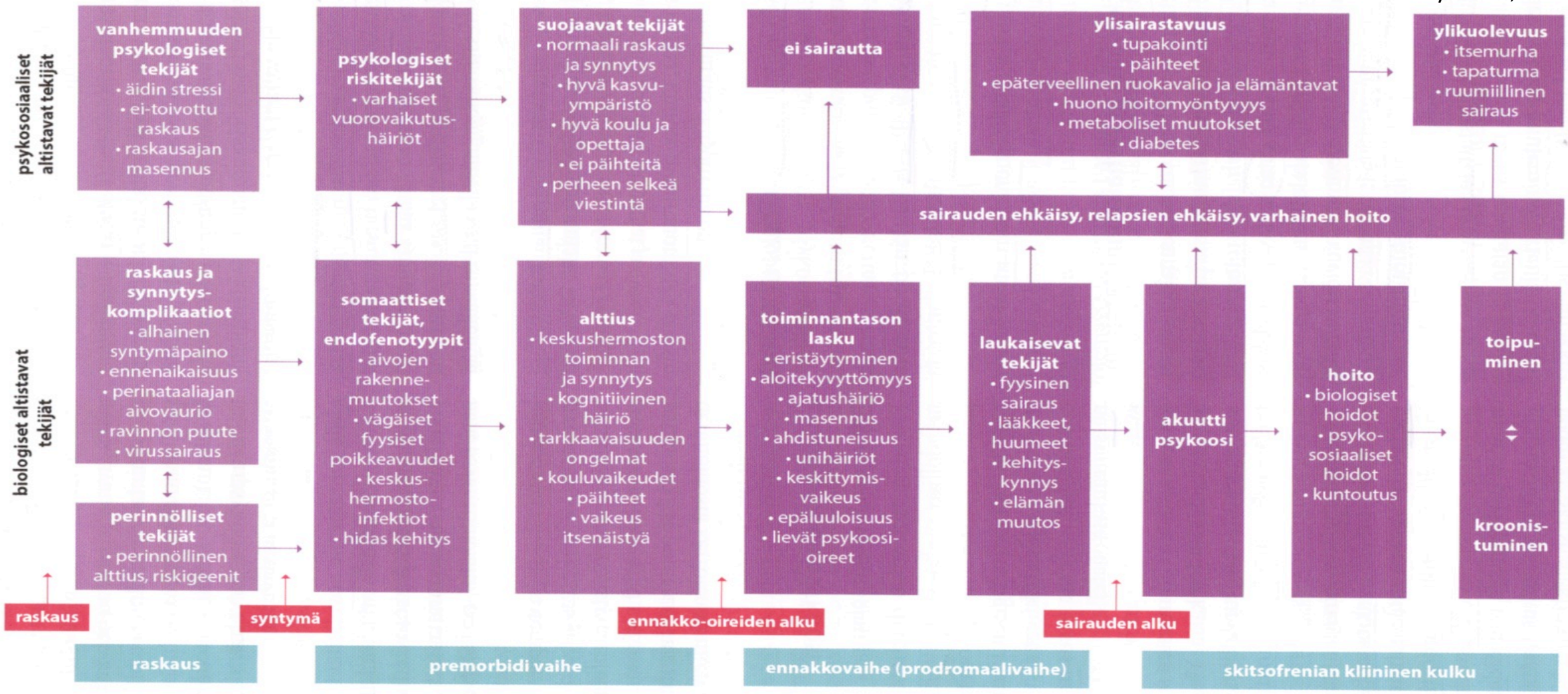
Table 3–3. Typical clinical characteristics of ultra-high-risk patients

- Attenuated psychotic symptoms, such as overvalued ideas, perceptual abnormalities, and mild thought disorder
- Lowered or unstable mood
- Social withdrawal
- Interpersonal difficulties, such as conflict with others or social cognition problems
- Self-harming behavior
- Substance misuse
- Functional difficulties, such as deterioration in school or work performance

Psykiatria, 2017



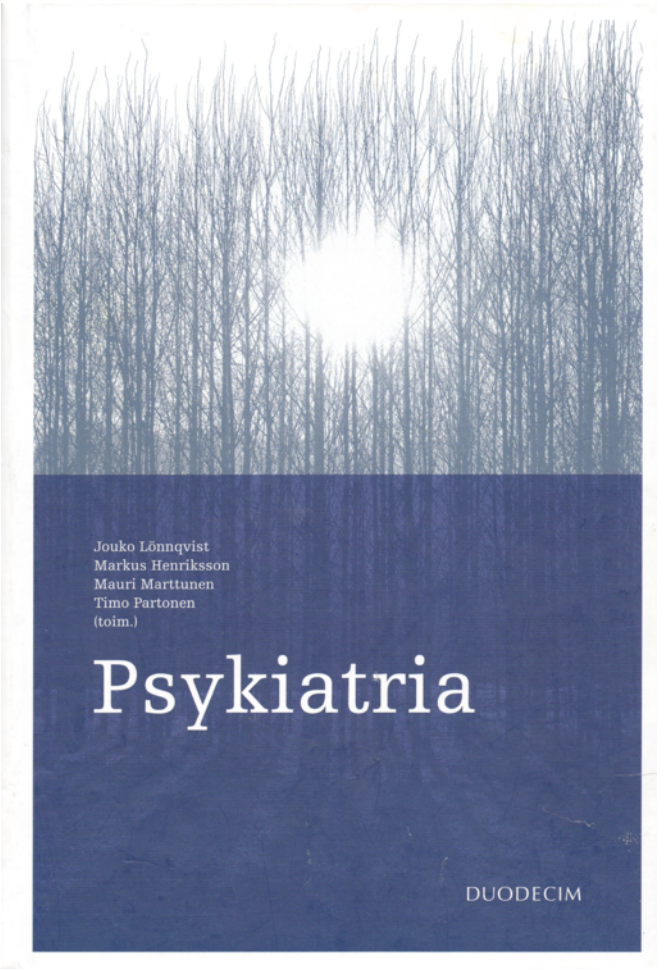
Kuva 3. Skitsofrenian kehitystä ja kulkua kuvaava elämänkaarimalli, jossa esitetään tunnettuja skitsofrenian riskitekijöitä. Nämä selittävät vain osan alttiudesta sairastua: suurin osa altistuneista ei sairastu. Riskitekijät ovat myös epäspesifisiä eli ne voivat altistaa muihin mielenterveyshäiriöihin. Suojaavista tekijöistä ei ole välttämättä näyttöä.

2. Skitsofrenian epidemiologiaa

Yl juha kemppinen

Taulukko 4. Skitsofrenian epidemiologiaa.

Elinaikainen sairastumisriski noin 1 %
Suomessa on noin 50 000 skitsofreniaa sairastavaa henkilöä.
Potilaan sisarilla ja veljillä sekä lapsilla sairastumisriski on 5–10-kertainen.
Vuosittain 10 000:ta henkilöä kohden ilmaantuu 0,8–4,3 uutta tapausta.
Suomessa esiintyvyys on suurin Itä- ja Pohjois-Suomessa.
Miehet sairastuvat yleensä 20–28 vuoden iässä.
Alle 30-vuotiaina sairastuneista kaksi kolmasosaa on miehiä.
Naiset sairastuvat yleensä 24–32 vuoden iässä.
Yli 40-vuotiaina sairastuneissa on enemmän naisia.
Potilaiden sosiaalinen asema ja opiskelu- sekä työkyky heikkenevät sairastumisen jälkeen.



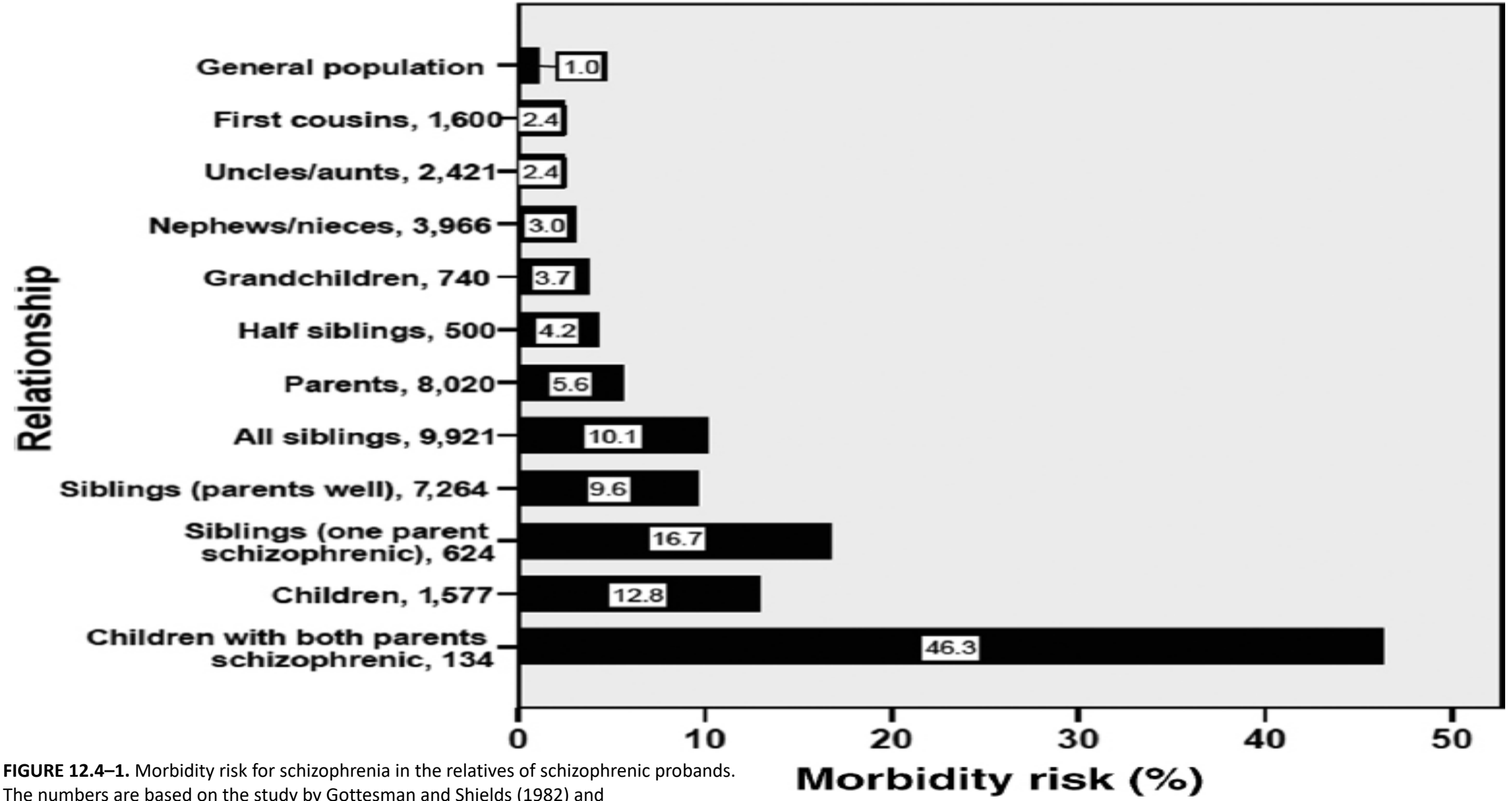


FIGURE 12.4–1. Morbidity risk for schizophrenia in the relatives of schizophrenic probands. The numbers are based on the study by Gottesman and Shields (1982) and used with permission by Irving Gottesman.

Kaplan&Sadock´s, 2017,10th ed

Taulukko 3. Skitsofrenian hyvään ja huonoon ennusteeseen liittyviä tekijöitä.

Hyvä ennuste	Huono ennuste
• Naissukupuoli • Myöhäinen alku • Laukaisevia tekijöitä • Nopea ja akuutti taudinkuva • Hyvä sairautta edeltävä koulutus ja ammatillinen toimintakyky • Hyvä sairautta edeltävä sosiaalinen toimintakyky • Sairaudentunto, hoitomyöntyvyys • Pääosin positiivisia oireita, mutta ei varhaisia aisti-harhoja tai harhaluuloja • Paranoidisia oireita ja masennusoireita • Ei neuropsykologisia häiriöitä tai aivojen rakenne-muutoksia • Parisuhde, perheen lämmin tunneilmapiiri ja hyvä sosiaalinen tukiverkosto • Nopea toipuminen ensipsykoosista • Varhainen ja hyvä hoito, asianmukainen lääkehoito	• Miessukupuoli • Perinnöllinen alttius • Sairastuminen nuorella iällä • Ei laukaisevia tekijöitä • Hidas alku, ennakko-oireita pitkään • Huono sairautta edeltävä selviäminen • Pääosin negatiivisia oireita • Samanaikaiset muut psykiatriset häiriöt: päihdehäiriö, masennus • Hajanaistyyppinen taudinkuva, varhaiset aistiharhat ja harhaluulot • Neuropsykologinen häiriö tai aivojen rakennemuutoksia • Ei parisuhdetta, perheen kriittinen tunneilmapiiri ja vähäinen sosiaalinen tuki • Pitkään kestänyt hoitamaton ensipsykoosi, huono vaste hoitoon • Hoidon puutteet (psykoosilääkitys, kuntoutus) • Huono hoidon jatkuvuus • Liiallinen lääkitys

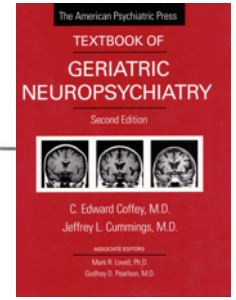


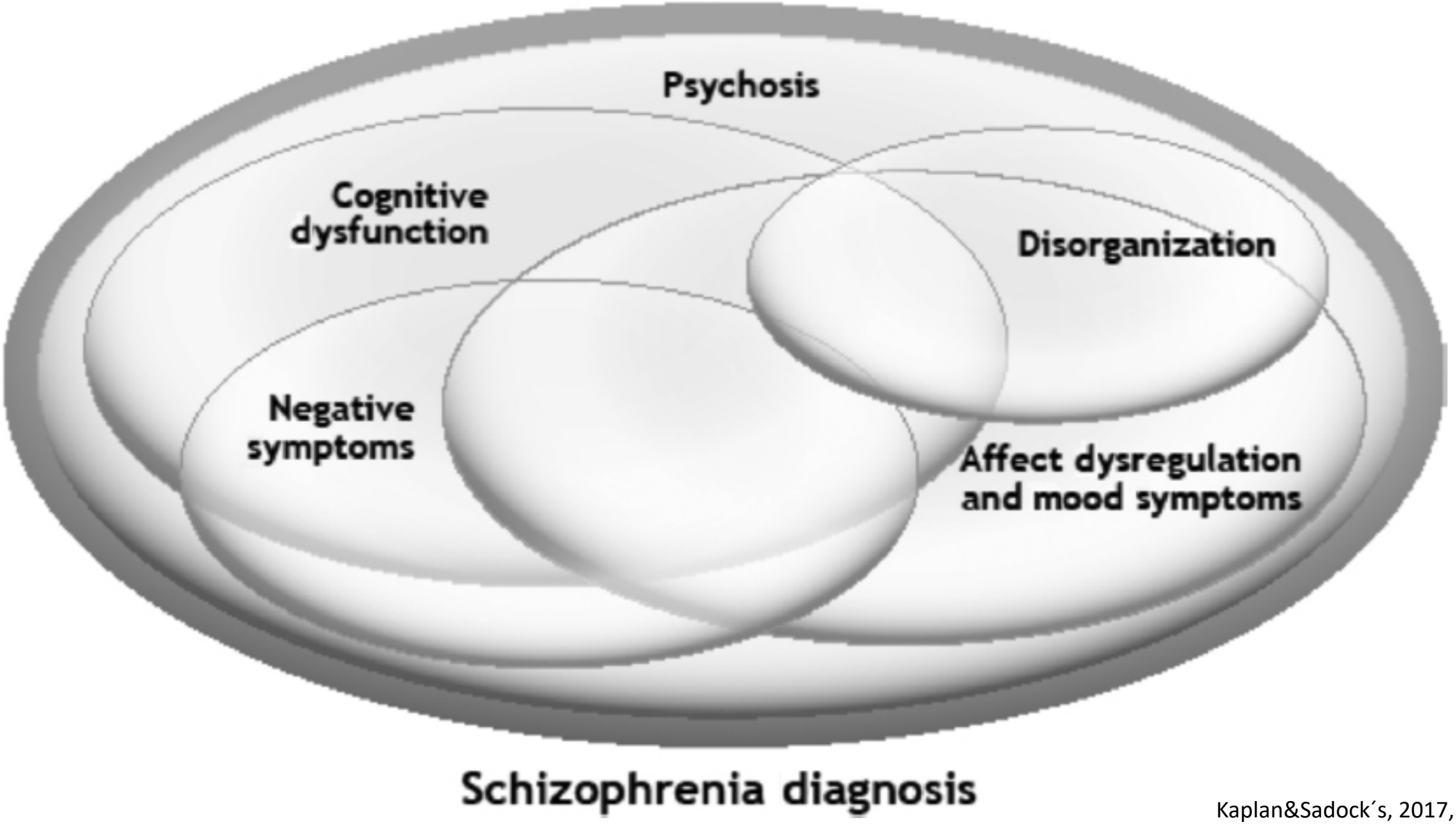
TABLE 14–1. Comparison of symptoms among young patients with early-onset, patients with late-life–onset, and elderly patients with early-onset schizophrenia

Symptoms	Young patients with early-onset schizophrenia	Patients with late-life–onset schizophrenia	Elderly patients with early-onset schizophrenia
Hallucinations	80% (Pearlson et al. 1989)	Present in 94%; more vivid in multiple modalities (Kay and Roth 1961; Pearlson et al. 1989)	100% (Pearlson et al. 1989)
Delusions	69% (Pearlson et al. 1989)	98% (Pearlson et al. 1989), especially persecutory (also Kay and Roth 1961)	100% (Pearlson et al. 1989)
Schneiderian first-rank symptoms	50% (Pearlson et al. 1989)	35% (Pearlson et al. 1989); thought insertion and withdrawal rarer than that in early-onset schizophrenia (Grahame 1984; Holden 1987)	41% (Pearlson et al. 1989)
Formal thought disorder	52% (Pearlson et al. 1989)	Rare (5.6%) (Pearlson et al. 1989); similar (Bleuler 1943; Gabriel 1978; Huber et al. 1975)	55% (Pearlson et al. 1989)
Negative symptoms	22% (Pearlson et al. 1989)	Rarer (e.g., Bleuler 1943; Castle and Howard 1992; Pearlson et al. 1989)	23% (Pearlson et al. 1989)

3. Skitsofrenian etiologiaa (neurobiologia)

Yl juha kemppinen

Symptom dimensions of schizophrenia



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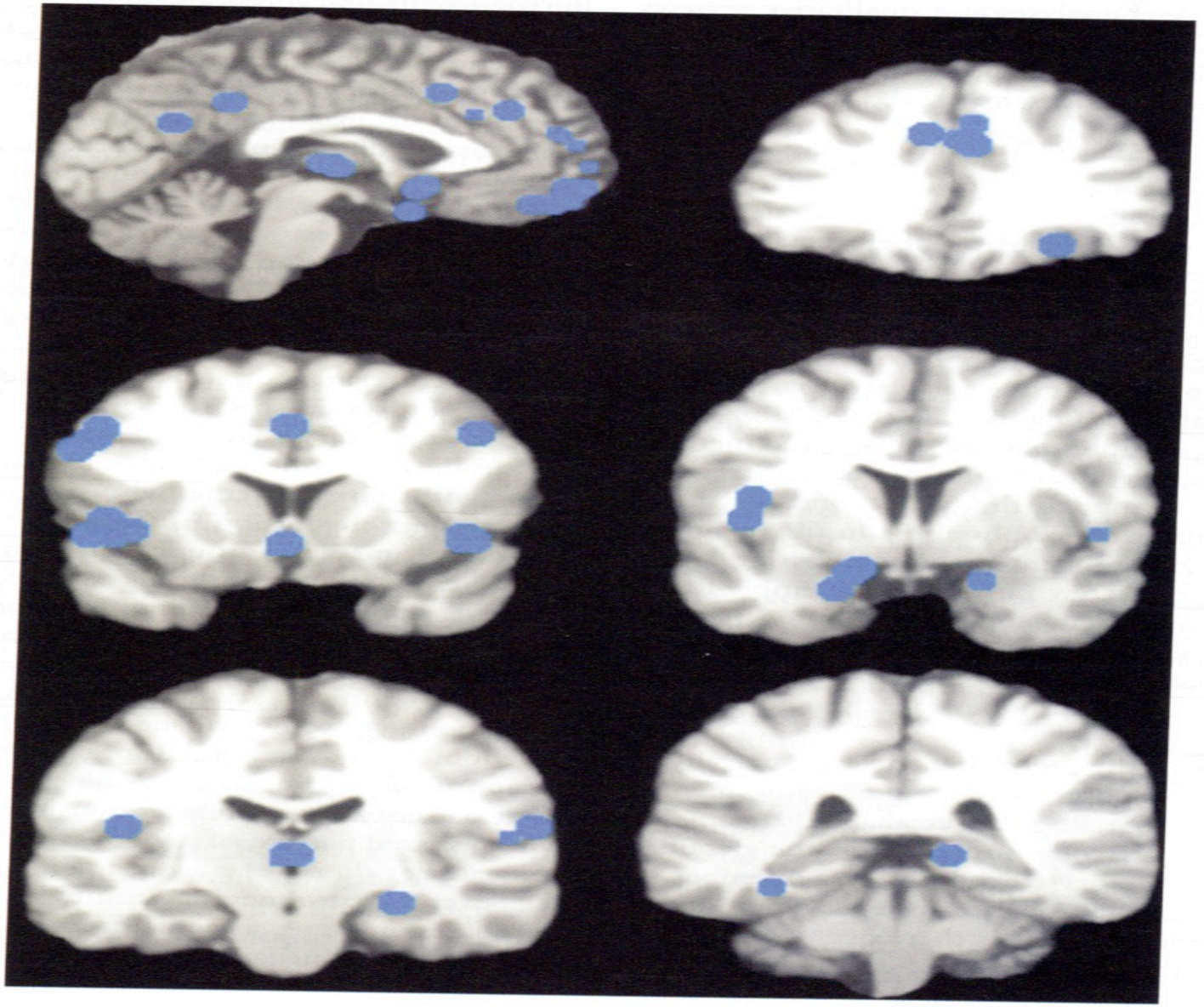


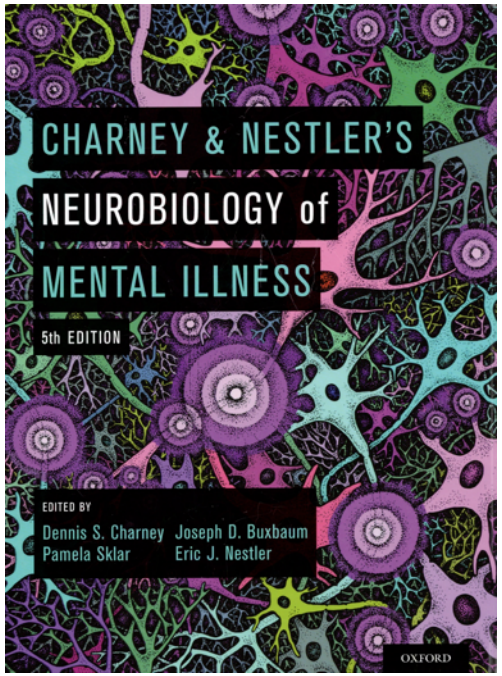
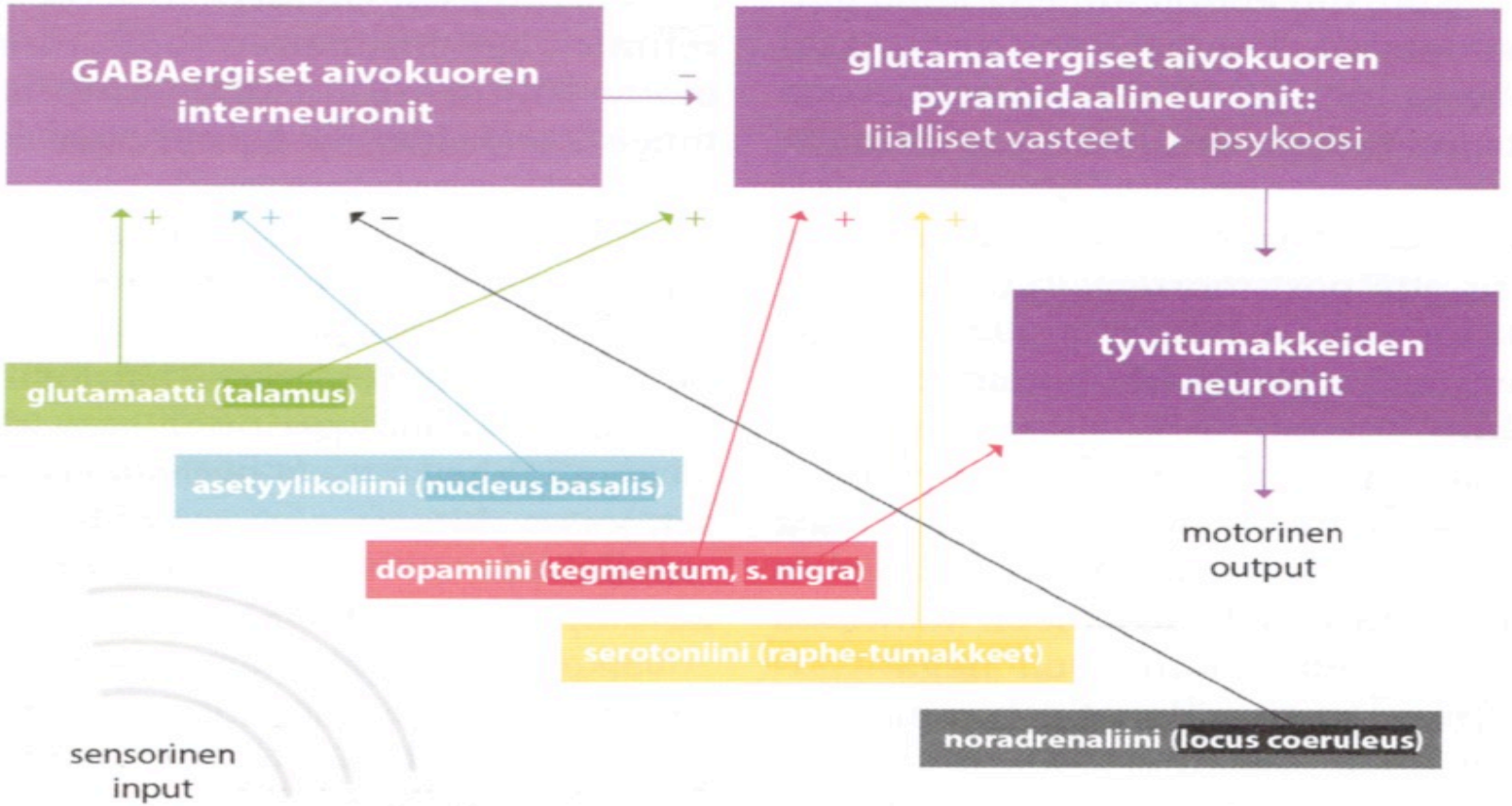


Figure 14.1 Reduced grey matter density in chronic schizophrenia. Dots indicate the spatial proximity of foci identified across multiple voxel-based meta-analyses, with coronal slices progressively posterior from left to right. Reproduced from Shepherd, A.M., et al., 2012. Systematic meta-review and quality assessment of the structural brain abnormalities in schizophrenia. *Neuroscience and Biobehavioral Reviews*. With permission from Elsevier.



Kuva 2. Yksinkertaistettu kaavio aivojen välittäjäainetoiminnasta psykoosioireilun kannalta, joka kuvastaa sitä miten monella tavalla tämän hermoverkon toimintaa voidaan moduloida. + tarkoittaa aktivaatiota ja – inhibitiota. Liialliset aivokuoren pyramidaalisolujen vasteet ovat oleellinen osa hermoverkon toimintaa, jonka ajatellaan johtavan psykoosioireiluun. Kuviosta voi päätellä, että antipsykoottisen vaikutuksen kannalta esim noradrenaliinin (alfa-2 reseptori välitteinen), serotoniinin(5-HT2a reseptori) ja dopamiinin (D2 reseptori) reseptorivaikutusten estäminen on hyödyllistä kun taas asetyylikoliinin nikotiiniresptorivaikutuksen lisääminen voisi olla hyödyllistä. Modifioitu Freedman 2003, Hietala ja Tuulio-Henriksson 2011.

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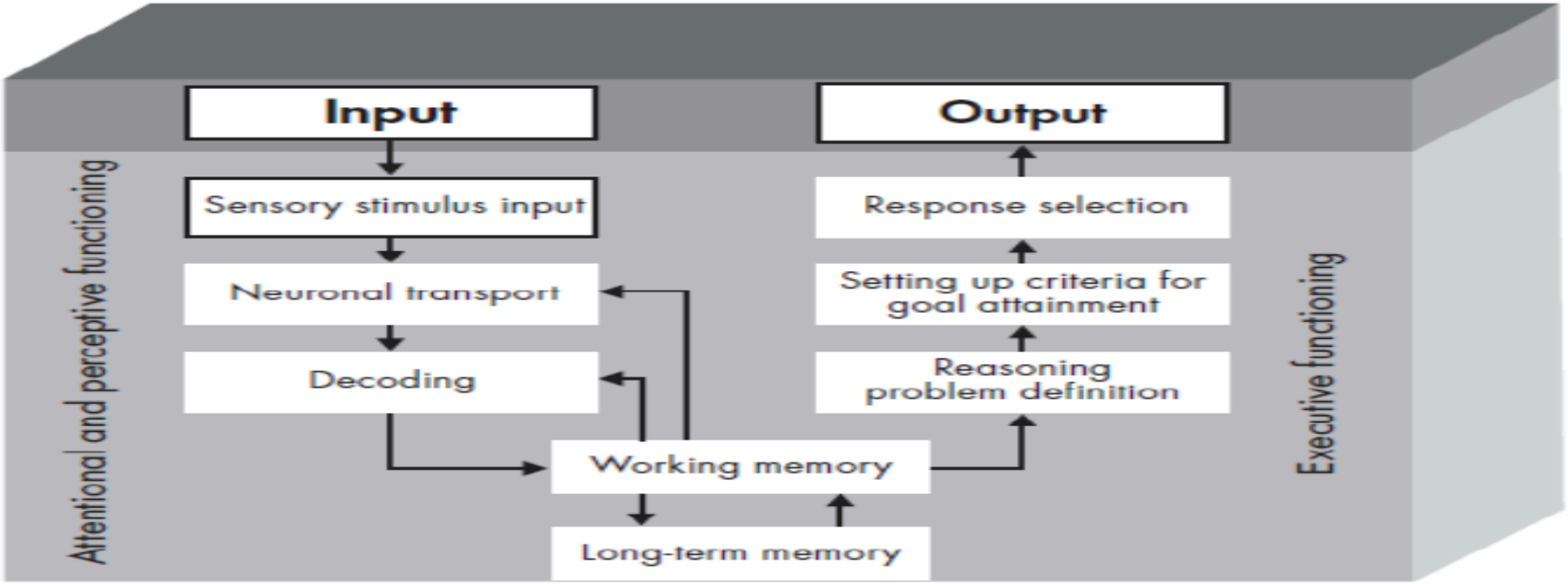

Figure 5–1. General model of information processing.
Source. Adapted from Roder et al. 2008.

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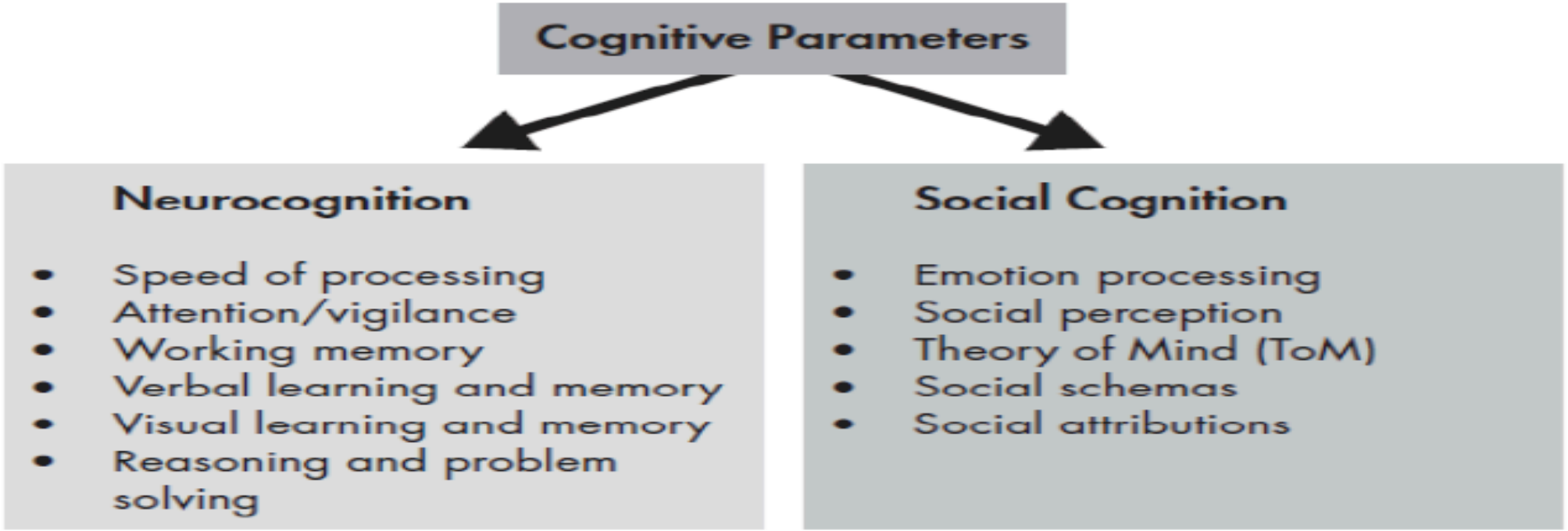

Figure 5–2. Cognitive parameters identified by the National Institute of Mental Health (NIMH) Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Initiative.
Source. Adapted from Green et al. 2005; Nuechterlein et al. 2004.

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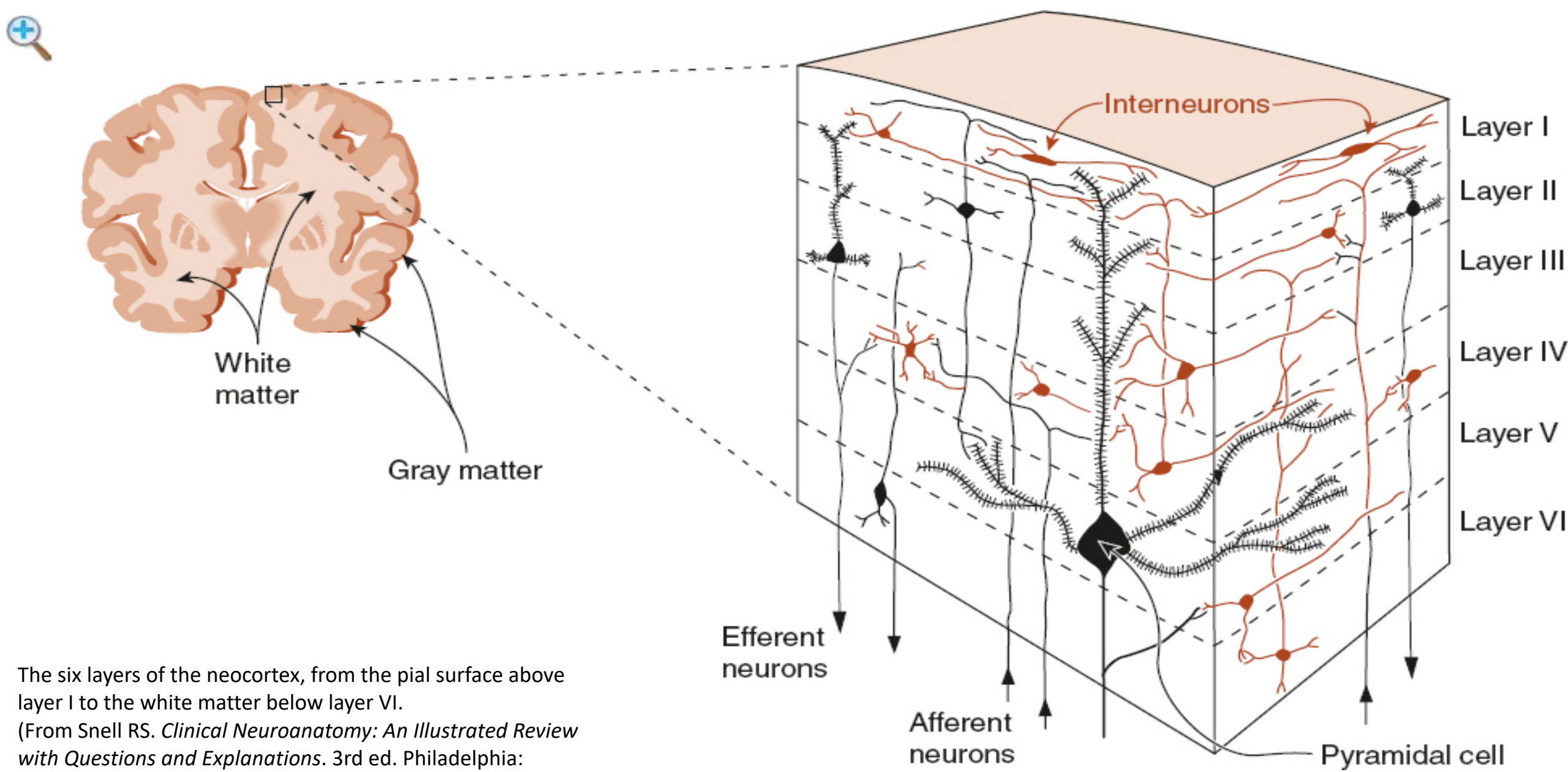
Table 5–1. MATRICS Consensus Cognitive Battery (MCCB)

Subdomain	Instrument(s)
Speed of processing	Brief Assessment of Cognition in Schizophrenia (BACS): Symbol-Coding
	Category Fluency: Animal Naming
	Trail Making Test: Part A
Attention/vigilance	Continuous Performance Test—Identical Pairs (CPT-IP)
Working memory	Wechsler Memory Scale—3rd Edition (WMS-III): Spatial Span (nonverbal)
	Letter-Number Span (verbal)
Verbal learning	Hopkins Verbal Learning Test—Revised (HVLT-R)
Visual learning	Brief Visuospatial Memory Test—Revised (BVMT-R)
Reasoning and problem solving	Neuropsychological Assessment Battery (NAB): Mazes
Social cognition	Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT): Managing Emotions

Note. MATRICS = Measurement and Treatment Research to Improve Cognition in Schizophrenia.
Source. Adapted from Green et al. 2008a; Nuechterlein et al. 2008.



The six layers of the neocortex, from the pial surface above layer I to the white matter below layer VI.
(From Snell RS. *Clinical Neuroanatomy: An Illustrated Review with Questions and Explanations*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.)

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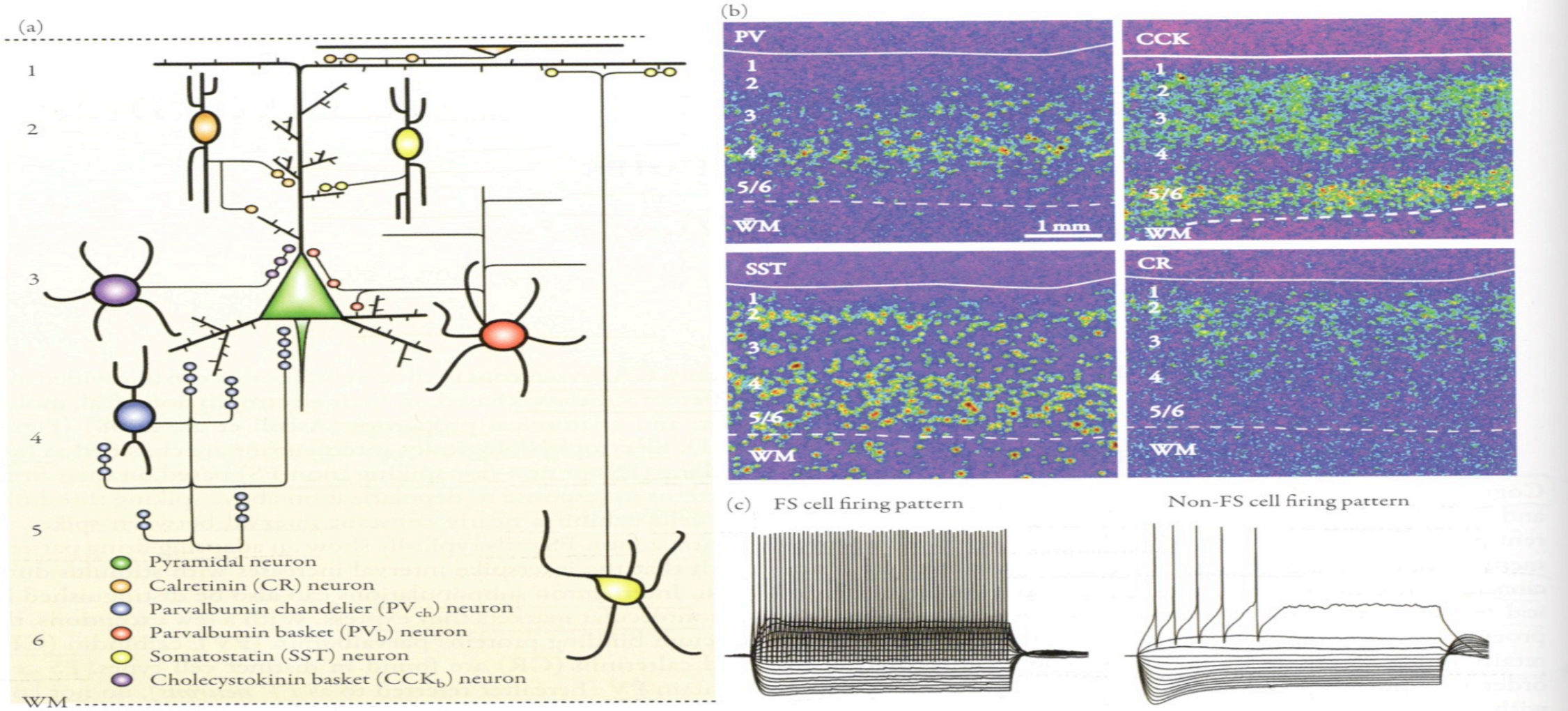


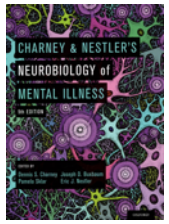


Figure 18.1 **Diversity of cortical GABA neurons**. GABAergic interneurons can be classified based on morphological (A), molecular (B), and electrophysiological (C) properties. Some interneurons express the calcium binding proteins parvalbumin (PV) or calretinin (CR), whereas others contain the neuropeptides somatostatin (SST) or cholecystokinin (CCK). (A) PV and CCK neurons target the perisomatic region of pyramidal cells, while SST and CR neurons target pyramidal neuron dendrites. PV neurons can be divided into chandelier (PV_{ch}) and basket (PV_b) cells based on their morphology. The axon terminals of PV_{ch} cells exclusively target the pyramidal cell axon initial segment, while the terminals of PV_b cells synapse onto the soma and proximal dendrites. (B) The different interneuron subtypes are distributed distinctively across the layers of the cortex, as evidenced by the different expression patterns of their mRNAs. (C) PV cells exhibit a fast spiking (FS) firing pattern, characterized by a high firing frequency and constant interval between action potentials, while the remaining subclasses are classified as non-FS cells that fire at a lower frequency and exhibit progressively increasing intervals between action potentials. Image adapted from Gonzalez-Burgos et al., 2007, and Hashimoto et al., 2008.

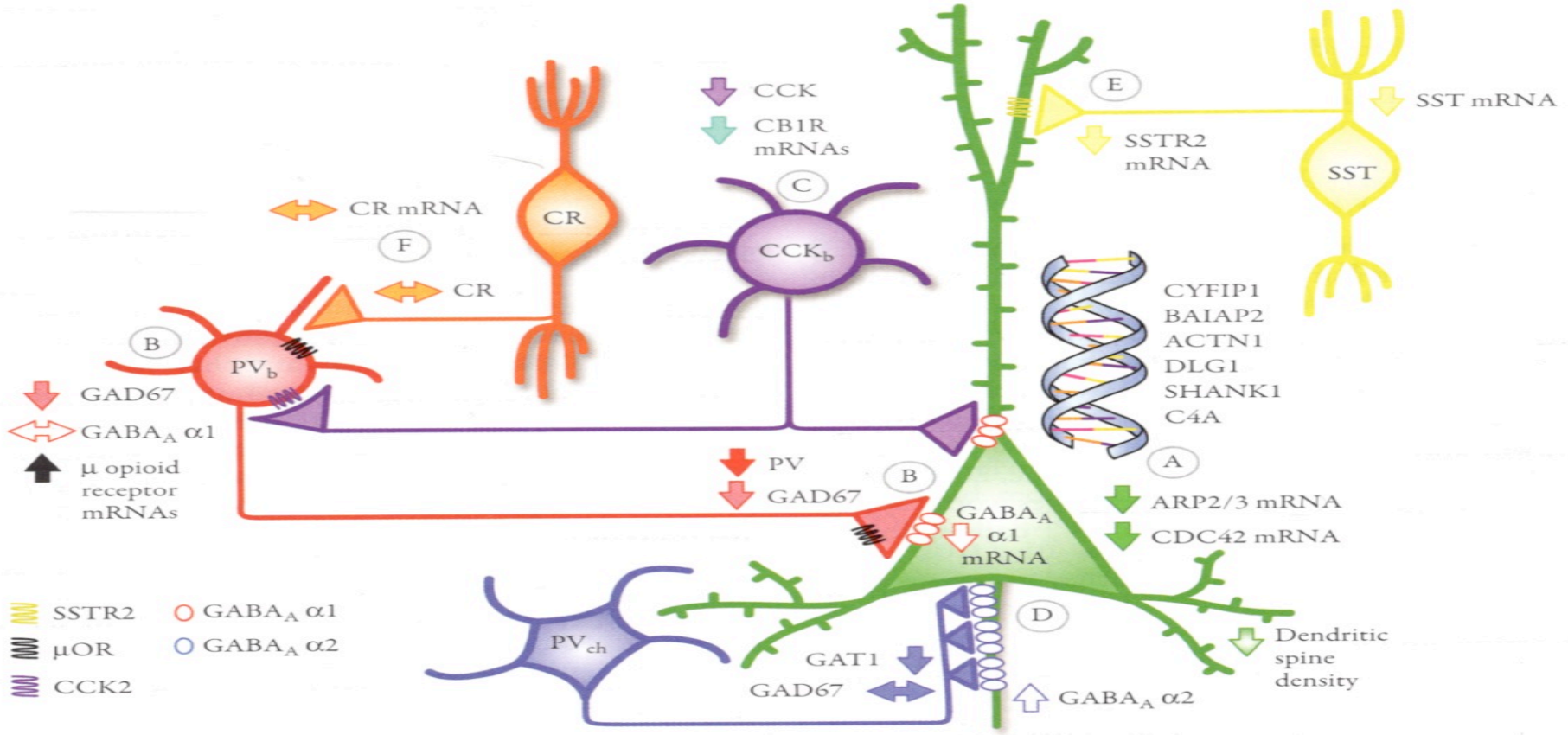
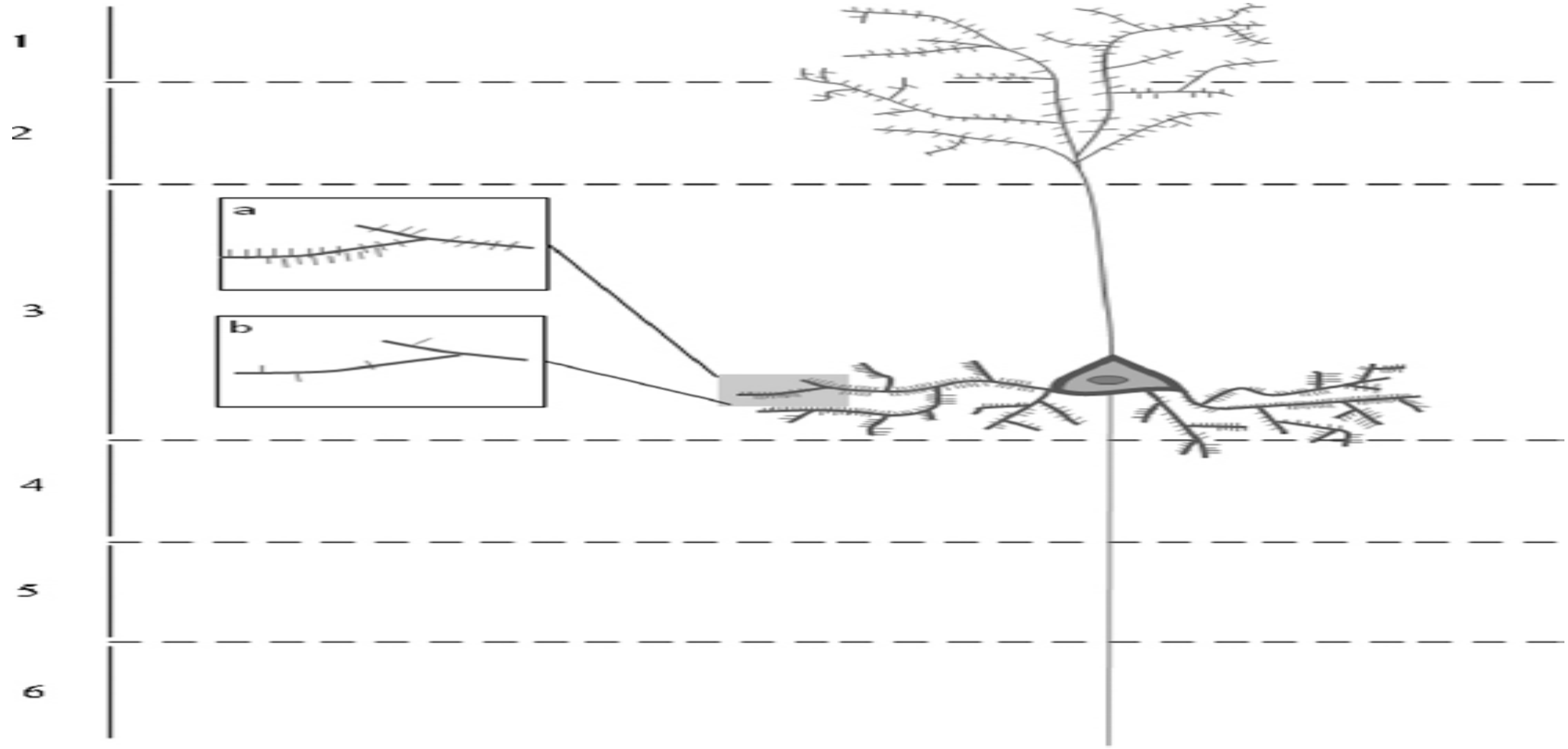


Figure 18.3 Schematic summary of alterations in neuronal circuitry in the PFC of subjects with schizophrenia. **(A)** Risk alleles and de novo mutations associated with schizophrenia are overrepresented at loci that contain genes, such as CYFIP1, BAIAP2, ACTN1, DLG1, SHANK1, and C4A, which influence actin dynamics and/or dendritic spine life cycle (Purcell et al., 2014; Sekar et al.,). These factors, in combination with alterations in the expression of other gene products that regulate the actin cytoskeleton, such as CDC42 and ARP2/3, could contribute to fewer dendritic spines on layer 3 pyramidal cells in schizophrenia. **(B)** These intrinsic alterations in pyramidal cells could lead to lower excitatory input to parvalbumin basket (PV_b) cells and a compensatory downregulation of inhibitory inputs from PV_b cells to pyramidal cells. The perisomatic inhibition of pyramidal neurons by PV_b cells is lower due to (1) lower GAD67 mRNA and protein, and therefore less GABA synthesis; (2) higher levels of μ opioid receptor expression in PV_b cells that reduces their activity and suppresses GABA release; (3) reduced expression of cholecystokinin (CCK) mRNA, which stimulates the activity of, and GABA release from, PV_b cells; and (4) less mRNA for, and presumably fewer, postsynaptic $GABA_A$ α1 receptors in pyramidal neurons. **(C)** The perisomatic inhibition of pyramidal neurons by cholecystokinin-expressing basket (CCK_b) cells is enhanced due to lower levels of CCK and cannabinoid 1 receptor (CB1R) mRNAs that reduce depolarization-induced suppression of inhibition (DSI). Levels of GAD67 in CCK_b cells are unknown but are thought to be low, relative to PV cells, in the healthy state. **(D)** PV-expressing chandelier (PV_{ch}) cells have lower GABA membrane transporter 1 (GAT1) protein in their axon terminals and higher postsynaptic $GABA_A$ α2-containing receptors at pyramidal neuron axon initial segments in individuals with schizophrenia. The levels of GAD67 protein in PV_{ch} cells in schizophrenia are unaltered. **(E)** Somatostatin (SST)-containing cells contain lower mRNA levels of SST, and expression of its receptor, SSTR2, in pyramidal cells is also lower. Levels of GAD67 in SST cells have not been measured. **(F)** Calretinin (CR)-containing cells are thought to be unaffected, since levels of CR mRNA and protein are unaltered. GAD67 levels in CR cells are unknown.

Schematic representation of dendritic spine density in layer 3 prefrontal cortex pyramidal neuron in controls (a) compared to schizophrenia (b).



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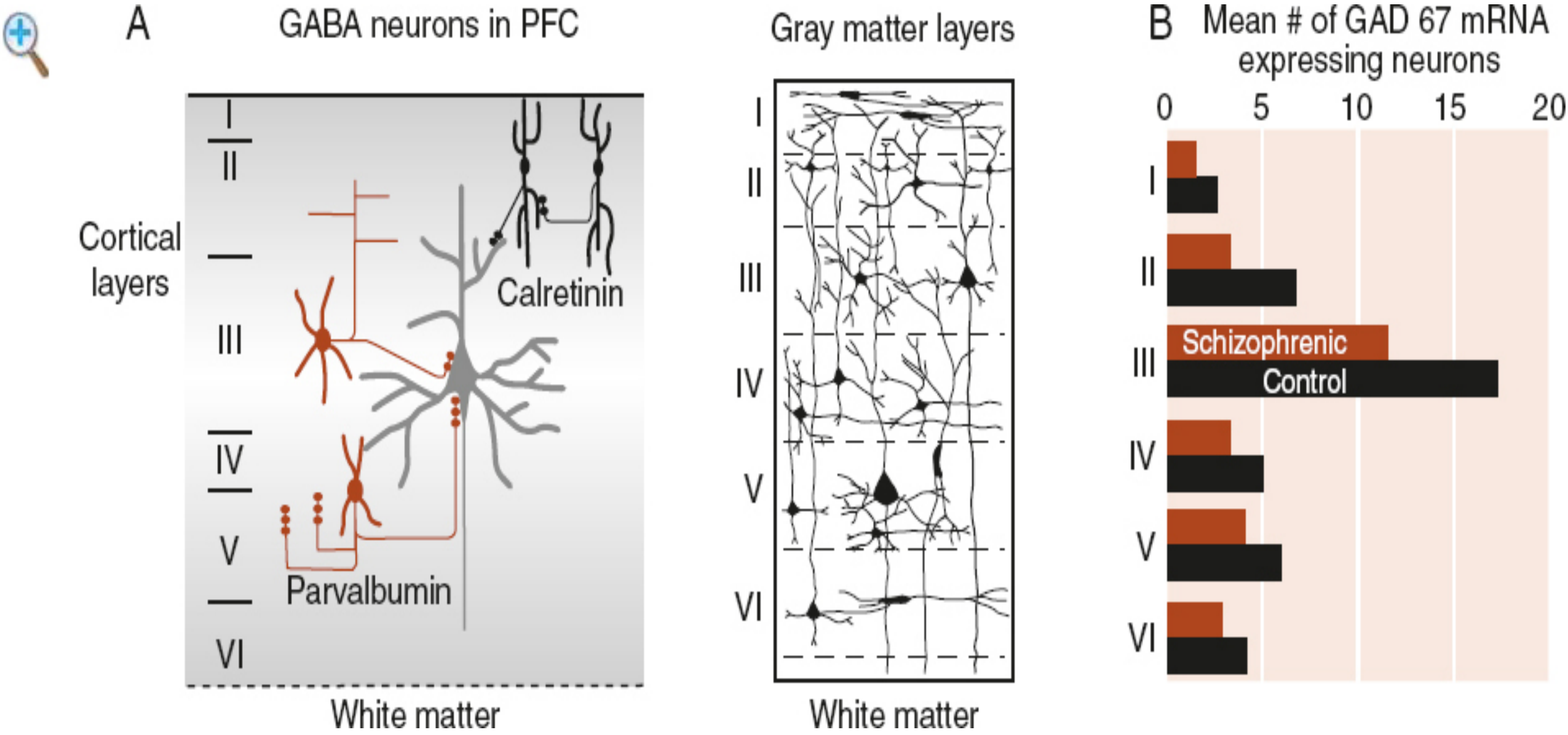

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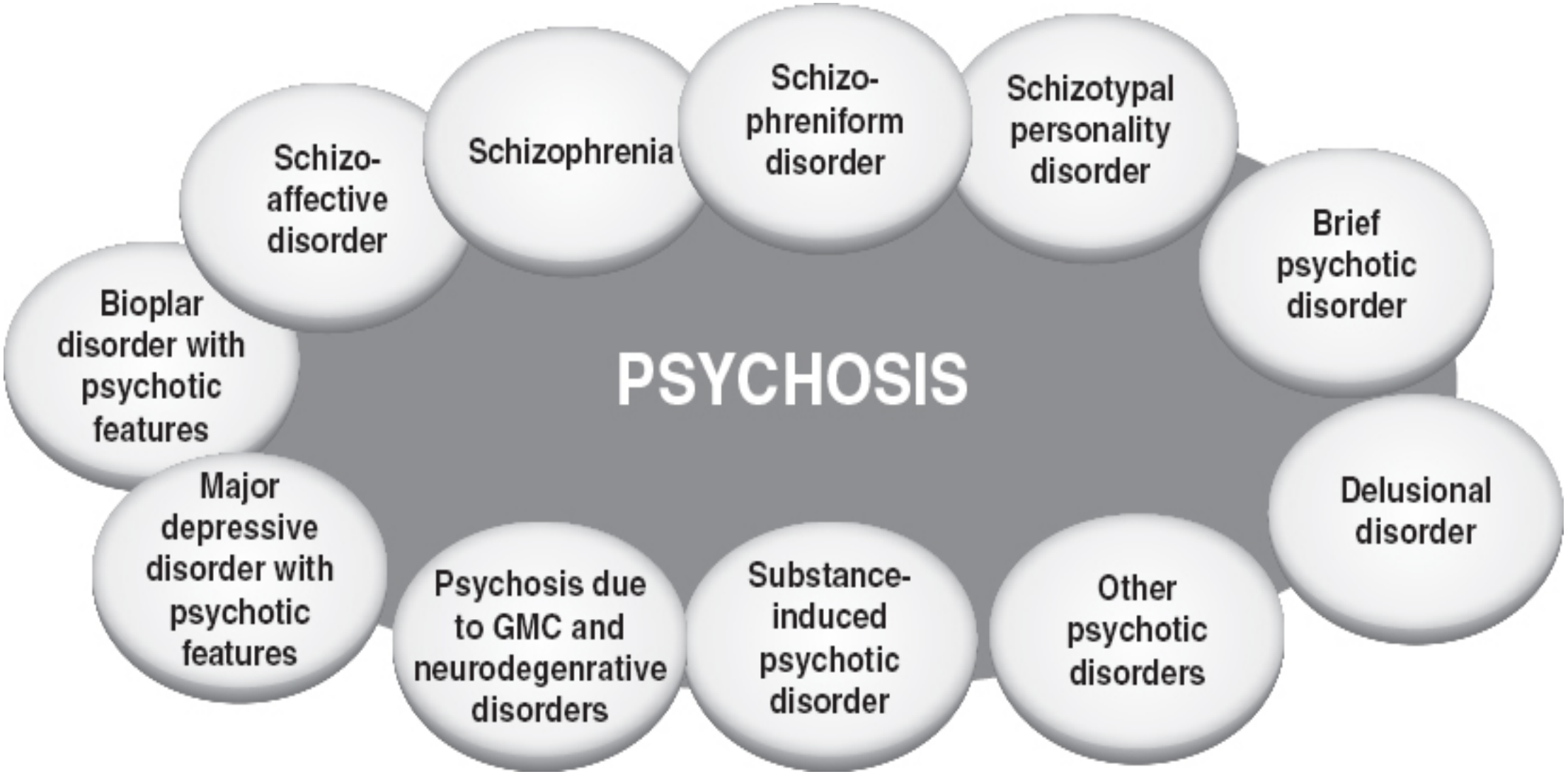
4. Skitsofrenian diagnosointi

Yl juha kemppinen

DSM-5 diagnoses overlapping the psychosis dimension. GMC, general medical conditions



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Taulukko 19. Muut psykoottiset häiriöt ICD-10:ssä.

F21	Skitsotyyppinen häiriö
F22	Pitkäaikaiset harhaluuloisuushäiriöt
F23	Äkilliset ja väliaikaiset psykoottiset häiriöt
F24	Indusoitunut harhaluuloisuus
F25	Skitsoaffektiiviset häiriöt
F28	Muut määritetyt ei-elimelliset psykoottiset häiriöt
F29	Määrittämätön ei-elimellinen psykoottinen häiriö
F00-19	Elimellisiin aivo-oireyhtymiin liittyvät ja lääkkeiden ja päihteiden aiheuttamat psykoosit

Taulukko 18. Miksi skitsofrenia pitäisi todeta ja hoitaa varhain?

Mitä etuja voidaan saavuttaa?

- Varhainen hoito parantaa ennustetta.
- Itsemurha vaara vähenee.
- Päihteiden käytön riski vähenee.
- keskushermostomuutosten, riski saattaa vähentyä.
- Sosiaaliset ongelmat, parisuhde, perhe, ystävät, koulu ja työ, eivät kärjisty.
- Omaisten hätä ja taakka helpottuvat.
- Hoito voi painottua avohoitoon.

Mikä estää varhaista hoitoa?

- Sairaus voi alkaa hitaasti.
- Oikea diagnoosi on joskus vaikea.
- Diagnostisia kriteereitä ei tunneta tai niitä ei haluta käyttää.
- Potilaan sairaudentunto tai muu kognitio voi olla puutteellinen.
- Potilaalla, omaisilla ja hoitavilla henkilöillä voi olla halu kieltää sairaus.
- Hoitojärjestelmä ja palvelurakenne eivät välttämättä tue varhaista hoitoa.

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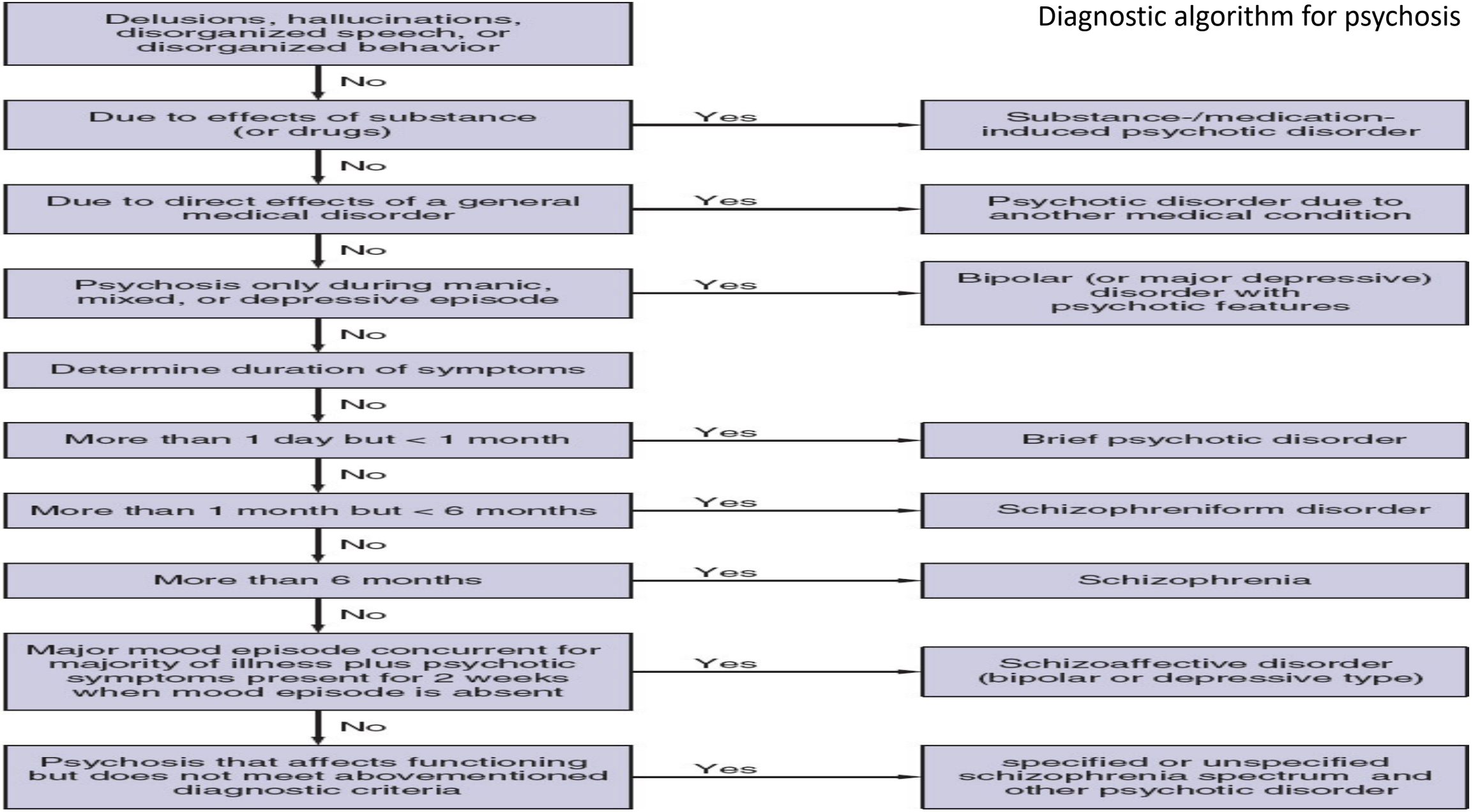
Table 4–1. DSM-IV-TR main diagnostic categories of psychotic disorders

Nonaffective psychotic disorders
Schizophrenia
Schizoaffective disorder
Schizophreniform disorder
Delusional disorder
Brief psychotic disorder
Psychotic disorder not otherwise specified
Affective psychoses
Bipolar disorder with psychotic features
Major depressive disorder with psychotic features
Substance-induced psychotic disorder
Alcohol-induced
Other substance-induced
Psychotic disorder due to a general medical condition

Source. American Psychiatric Association 2000.

Diagnostic algorithm for psychosis



McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

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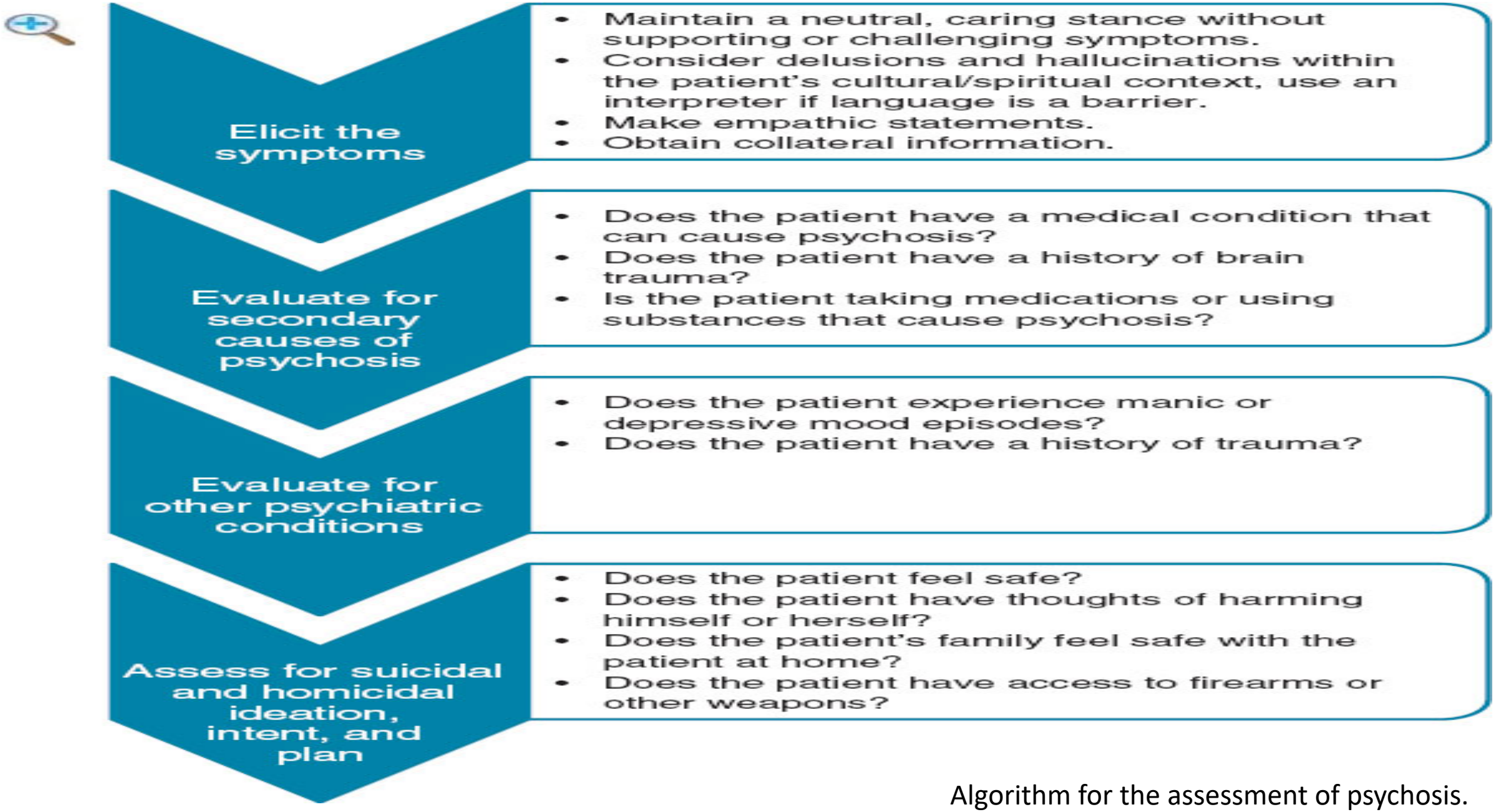
Table 4–6. Strategies for person-centered clinical evaluation

- Assess insight level and its variations during the course of the disorder.
- Pay attention to biographical and anamnestic aspects.
- Evaluate the risk of suicidality.
- Reinforce the adaptive insight.
- Analyze and improve coping resources.
- Identify risk factors for nonadherence and assess patient's attitude toward medication.
- Pay attention to and try to improve patient's subjective well-being while reducing symptoms.
- Include family relationships in the assessment as well as how the family members cope with the ill subject.
- Reinforce the adaptive coping.



Algorithm for the assessment of psychosis.

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

GOAL	WHAT YOU MIGHT SAY
Normalize	•"In my practice, many patients have experienced (symptom); have you experienced this as well?" •"Having schizophrenia is very common. In fact, 1% of people in the United States have schizophrenia at some point in their lives."
Empathize, don't collude	•"If it's all right, I would like to learn more about how the voices affect your life."
Ask, don't tell	•"How do you feel when this happens?" *or* "How do you cope when this happens?" is usually better than "I'd be scared if that happened to me," or "This sounds frightening," unless the patient is indicating a particular emotional state.
Validate, without confirming reality of the patient's symptoms	•*Patient*: "You believe me, don't you, doctor? Can't you see them too?" •*Doctor:* "I believe that these symptoms are very real and troubling to you, and I do not think you are making things up."

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

GOAL	WHAT YOU MIGHT SAY
Bring up psychotic symptoms in context of more normal experiences	•"The brain is very powerful, and we all have a strong mind–body connection. Have you ever cried or laughed when you watched a movie? Nothing was happening to you when you cried, but you were sad. Your mind lets you experience that sadness, and told you that you were sad. Similarly, your mind has you experiencing voices and visions that others aren't experiencing. Does that make sense?"
Discussing diagnosis: inquiry and biases	•"Have you heard of the term *hallucination* or *delusion*? What does that mean to you? What do you know about people who experience this? What happens to them?"
Preparation of key messages	•For any discussion of diagnosis or prognosis, prepare your key statements in advance. What are the three concise things that you want your patient and their family members to remember? For instance: • "You have a disease called schizophrenia." • "It is common and has many treatments. Together, we'll find the best treatment for you." • "With the right treatment, many people enjoy a good quality of life."

McCarron et al, Primary Care Psychiatry, 2019, 2nd ed

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Table 4–7. Classification of coping strategies in schizophrenia

Problem centered	Compensatory activities of the subject directly aimed to modify or eliminate the sources of distress
Non–problem centered	Compensatory activities of the subject characterized by keeping distance, passive avoidance, or suppression
	Ineffective and not focused on the true stress source or on improvement of the subject's stress response
Behavioral	Characterized by observable behavior
Cognitive	Characterized by inner adaptation or compensatory cognitive processes
Emotional	Characterized by affective adaptation

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Table 6–1. Characteristic negative symptoms of schizophrenia

Symptom type	Clinical manifestation
Flattened affect	Unchanging facial expression, vocal tone, body position
Alogia	Lessening of speech fluency; reduced capacity to initiate or respond to speech; meager or impoverished content of speech
Avolition	Passivity; reduced capacity to initiate willful action
Apathy	Loss of interest; emotional disengagement; lack of spontaneity
Anhedonia	Lack of enjoyment in life; inability to experience pleasure or intimacy
Asociality	Social isolation due to active or passive social withdrawal
Psychomotor retardation	Slow or restricted physical movement
Impaired attention	Poor mental focus; poor persistence at tasks

Source. Adapted from Möller 2007.

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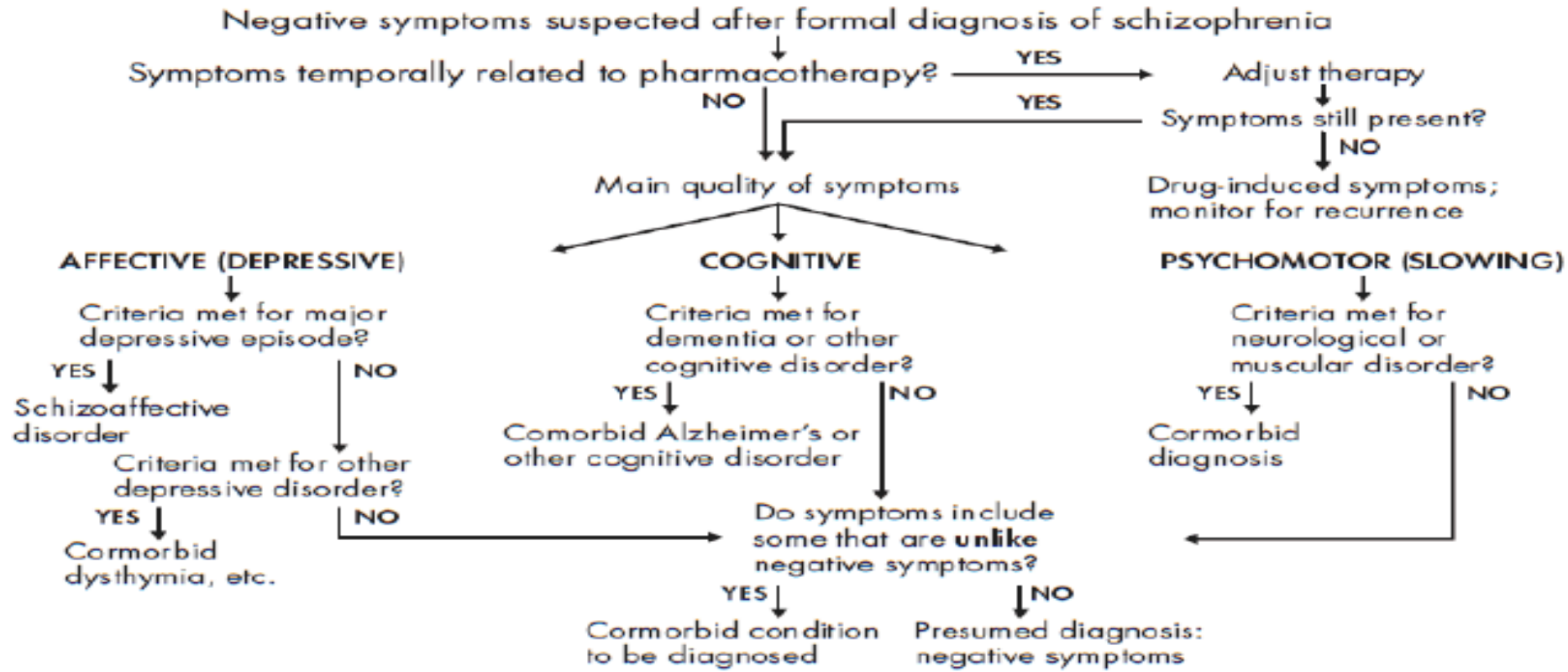

Figure 6–2. Algorithm for the differential diagnosis of negative symptoms in schizophrenia.

Source. Adapted from Möller 2007.

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Table 6–4. Items of the Calgary Depression Scale for Schizophrenia

CDSS

1. Depressed mood
2. Hopelessness
3. Self-deprecation
4. Guilty ideas of reference
5. Pathological guilt
6. Morning depression
7. Early awakening
8. Suicide
9. Observed depression

Source. Addington et al. 1990.

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Table 6–6. Specific risk factors for suicide in schizophrenia

- Previous depressive disorder
- History of suicide attempt
- Hopelessness
- Poor adherence to treatment
- Higher educational attainment
- Age≥30 years at onset of symptoms

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Table 6–7. SAD PERSONAS Scale for assessment of suicide risk

S ex[a]

A ge[b]

D epression

P revious attempt

E thanol and drug abuse

R ational thought loss

S ocial supports lacking

O rganized plan

N o spouse

A ccess to lethal means

S ickness

[a]Men account for 75% of suicide deaths; women attempt suicide more often than men.
[b]Elderly people and young adults are at greatest risk for suicide.
Source. Adapted from Patterson et al. 1983.

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Table 6–8. Co-occurrence of anxiety disorders in schizophrenia: overall prevalence rates

	OCD	PD	AGO	PTSD	SP	SPP	GAD	Any
No. of studies	34	23	12	20	16	11	14	16
No. of patients	3,007	1,393	862	1,388	1,259	925	939	958
Mean prevalence rate (%)[a]	12.1	9.8	5.4	12.4	14.9	7.9	10.9	38.3
95% CI	7.0%–17.1%	4.3%–15.4%	0.2%–10.6%	4.0%–20.8%	8.1%–21.8%	1.9%–13.8%	2.9%–18.8%	26.3%–50.4%
Range	0.6%–55.0%	0.0%–35.0%	0.0%–27.5%	0.0%–51.4%	3.6%–39.5%	0.0%–30.8%	0.0%–45.0%	10.4%–85.0%
Heterogeneity	317.98*	162.79*	83.52*	294.09*	127.37*	80.78*	142.52*	146.23*

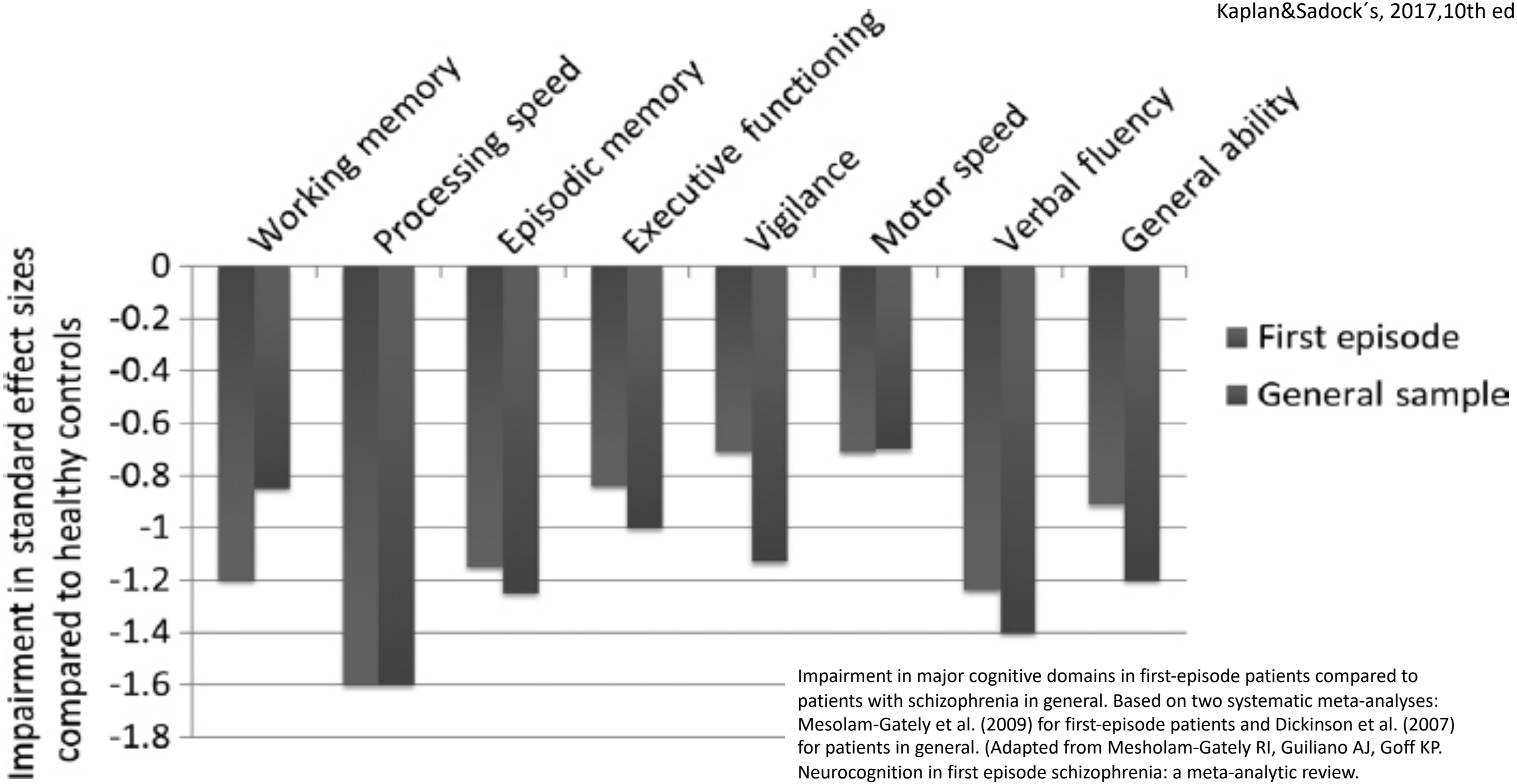
Note. AGO = agoraphobia; Any = proportion of patients with at least one of the anxiety disorders assessed in the study; CI = confidence interval; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PD = panic disorder; PTSD = posttraumatic stress disorder; SP = social phobia; SPP = simple phobia.

[a]Mean prevalence rates express main results.

*$P < 0.001$.

Source. Adapted from Achim et al. 2011.

Kaplan&Sadock´s, 2017,10th ed



Impairment in major cognitive domains in first-episode patients compared to patients with schizophrenia in general. Based on two systematic meta-analyses: Mesolam-Gately et al. (2009) for first-episode patients and Dickinson et al. (2007) for patients in general. (Adapted from Mesholam-Gately RI, Guiliano AJ, Goff KP. Neurocognition in first episode schizophrenia: a meta-analytic review. *Neuropsychology*. 2009;23:315–336; Dickinson D, Ramsey ME, Gold JM. Overlooking the obvious: a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Arch Gen Psychiatry*. 2007;64:532–542.)

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- **DSM-5:**
- **Schizophrenia Spectrum and Other Psychotic Disorders**
- The following specifiers apply to Schizophrenia Spectrum and Other Psychotic Disorders where indicated:
- [a] Specify if: The following course specifiers are only to be used after a 1-year duration of the disorder: First episode, currently in acute episode; First episode, currently in partial remission; First episode, currently in full remission; Multiple episodes, currently in acute episode; Multiple episodes, currently in partial remission; Multiple episodes, currently in full remission; Continuous; Unspecified
- [b] Specify if: With catatonia (use additional code 293.89 [F06.1])
- [c] Specify current severity of delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, negative symptoms, impaired cognition, depression, and mania symptoms

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- 301.22 (F21) Schizotypal (Personality) Disorder
- 297.1 (F22) Delusional Disorder[a, c]
- Specify whether: Erotomanic type, Grandiose type, Jealous type, Persecutory type, Somatic type, Mixed type, Unspecified type
- Specify if: With bizarre content
- 298.8 (F23) Brief Psychotic Disorder[b, c]
- Specify if: With marked stressor(s), Without marked stressor(s), With peripartum onset
- 295.40 (F20.81) Schizophreniform Disorder[b, c]
- Specify if: With good prognostic features, Without good prognostic features
- 295.90 (F20.9) Schizophrenia[a, b, c] ____.__ (____.__)
- Schizoaffective Disorder[a, b, c]
- Specify whether:295.70 (F25.0) Bipolar type
- 295.70 (F25.1) Depressive type
- ____.__ (____.__)
- Substance/Medication-Induced Psychotic Disorder[c]
- **Note:** See the criteria set and corresponding recording procedures for substance-specific codes and ICD-9-CM and ICD-10-CM coding.
- Specify if: With onset during intoxication, With onset during withdrawal

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- ____.__ (____.__)
- Psychotic Disorder Due to Another Medical Condition[c]
- Specify whether:
- 293.81 (F06.2)
- With delusions
- 293.82 (F06.0)
- With hallucinations
- 293.89 (F06.1)
- Catatonia Associated With Another Mental Disorder (Catatonia Specifier)
- 293.89 (F06.1)
- Catatonic Disorder Due to Another Medical Condition
- 293.89 (F06.1)
- Unspecified Catatonia
- **Note:** Code first **781.99 (R29.818)** other symptoms involving nervous and musculoskeletal systems.
- 298.8 (F28)
- Other Specified Schizophrenia Spectrum and Other Psychotic Disorder
- 298.9 (F29)
- Unspecified Schizophrenia Spectrum and Other Psychotic Disorder

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Measurement of the Neurocognitive Dimension

Neurocognitive dysfunctions are not part of the diagnostic criteria in DSM-IV-TR, even if it is now fully accepted that they represent not only a core aspect of the disorder but also candidate endophenotype features. Cognitive disturbances are highly prevalent and clinically severe in individuals with a diagnosis of schizophrenia (Keefe et al. 2005) and include difficulties concerning concentration and memory. These symptoms may be evident as follows:

- Slow thinking
- Difficulty in understanding
- Poor concentration
- Poor memory
- Difficulty in expressing thoughts
- Difficulty in integrating thoughts, feelings, and behavior
- Language communication difficulties
- Difficulty in decision-making processes

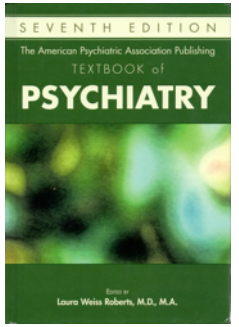
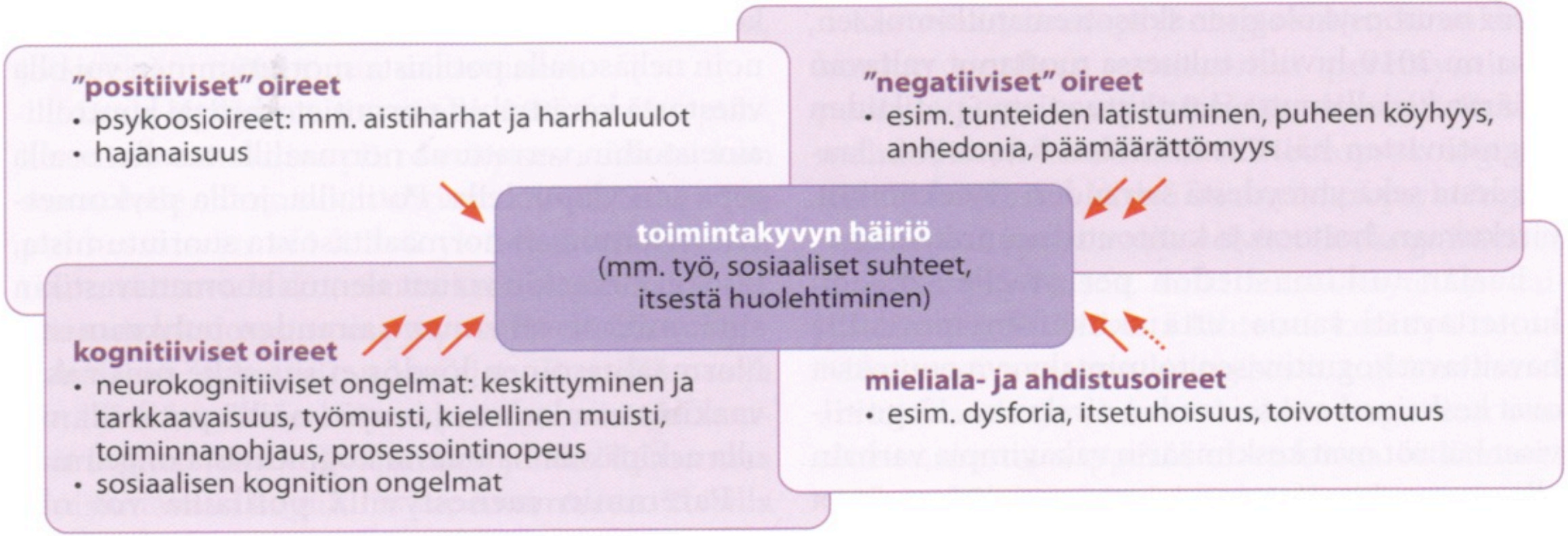


TABLE 10–3. Brief comparison of psychotic disorders

Disorder	Characteristics suggestive of the diagnosis	Symptom onset and duration
Schizophrenia	Prodromal phase with nonspecific symptoms is followed by enduring symptoms in multiple domains (positive, negative, disorganization, or cognitive).	Symptoms last more than 6 months.
Schizoaffective disorder	Symptoms resemble schizophrenia, but affected persons may not have impaired social or occupational functioning.	Psychotic symptoms are continuously present for more than 6 months, and depression or bipolar mood symptoms are present more than half of the time.
Schizophreniform disorder	Persons may not have impaired social or occupational functioning.	Symptoms last from 1 to 6 months.
Brief psychotic disorder	The onset is sudden, with no prodromal phase.	Symptoms last more than 1 day but resolve within 1 month.
Delusional disorder	Functioning is not impaired, and behavior is not odd, aside from the impact of the delusion.	Symptoms last more than 1 month.
Bipolar mania or depression with psychotic features	Content can vary but may be mood congruent.	Psychosis occurs only during the mood episode.



Kuva 1. Skitsofrenia oireyhtymänä. Kuvassa näkyvät sairauden keskeiset oiredimensiot. Mikään näistä oiredimensioista ei ole spesifinen skitsofrenialle, eivätkä ne ole toisistaan täysin riippumattomia. Esimerkiksi psykoosioireiden lisääntyessä myös mielialaoireet usein lisääntyvät. Kukin oiredimensio heikentää toimintakykyä ja elämänlaatua. Nuolien määrä kuvaa keskimääräistä vaikutusta potilaan ennusteeseen. Runsas kognitiivinen ja negatiivinen oireisto liittyvät huonoon ennusteeseen, sillä olemassa olevat hoitokeinot tepsivät niihin melko huonosti.

APA, 2019

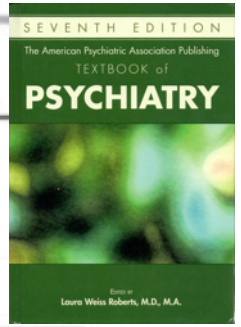


TABLE 10–1. Common schizophrenia symptoms

Positive symptoms	Negative symptoms	Disorganization	Cognitive impairment
Hallucinations	Flat affect	Disorientation	Slow processing speed
Hyperactivity	Reduced speech and activity	Bizarre posturing	Memory and learning deficits
Hypervigilance	Reduced social engagement	Illogical behavior	Poor executive function
Mood lability	Anhedonia	Poor attention	Poor social cognition
Grandiosity		Inappropriate affect	Difficulties with abstract thinking
Suspiciousness			
Hostility			

Note. Symptoms must be present for at least 6 months for an individual to receive a diagnosis of schizophrenia.

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Table 4–2. Differential diagnosis and medical causes of psychosis

Neurological	Pharmacological
Trauma	Antivirals
Multiple sclerosis	Anticonvulsants
Huntington's chorea	Anticholinergics
Epilepsy	Baclofen
Strokes	β-Blockers
Tumor	Bromocriptine
Abscesses	Cephalosporins
Normal pressure hydrocephalus	Captopril
Subarachnoid hemorrhage	Cimetidine
Intraparenchymal hemorrhage	Clonidine
Auditory or optic nerve disease	Corticosteroids
Fabry's disease	Disulfiram
Fahr's disease	Fluoroquinolones
Wilson's disease	Methotrexate
Parkinson's disease	Nonsteroidal anti-inflammatory drugs

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- **Metabolic and endocrine**
  - Cushing's syndrome
  - Hyperthyroidism
  - Hypothyroidism
  - Acute intermittent porphyria
  - Shock
  - Renal failure
  - Hepatic failure
  - Electrolyte imbalance
  - B_{12} deficiency
  - Addison's disease
  - Paraneoplastic syndrome
  - Systemic lupus erythematosus
  - Theophylline
  - Vincristine
- **Substance abuse**
  - Alcohol
  - Amphetamines
  - Belladonna alkaloids
  - Cannabis
  - Cocaine
  - Lysergic acid diethylamide
  - Phencyclidine
- **Infections and toxins**
  - Syphilis
  - Herpes encephalitis
  - HIV/AIDS
  - Creutzfeldt-Jakob disease
  - Lyme disease
  - Meningitis
  - Malaria
  - Heavy metal poisoning
  - Carbon monoxide poisoning

Source. Adapted from Hilty et al. 1999.

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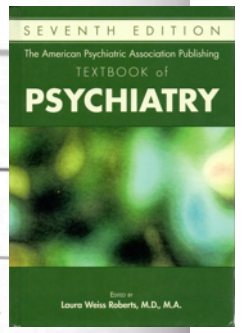

TABLE 10–2. Medical differential diagnosis: conditions that can result in psychosis

Medical condition	Considerations
Neoplasms	Mental status changes are common in primary and metastatic brain tumors.
Neurovascular events	Hemineglect and seizures can resemble delusions.
Seizures	Temporal lobe seizures can be associated with olfactory hallucinations and religious delusions.
Neurodegenerative disorders	Dementia, Huntington's disease, and Creutzfeldt-Jakob disease are all associated with psychosis.
White matter diseases	Metachromatic leukodystrophy, X-linked adrenoleukodystrophy, Pelizaeus-Merzbacher disease, cerebrotendinous xanthomatosis, adult-onset Niemann-Pick type C, and multiple sclerosis may be associated with symptoms of psychosis.
Systemic lupus erythematosus	Psychosis occurs in 5%–15% of patients.
Delirium	Electrolyte disturbances and poor oxygenation associated with many illnesses may cause psychosis. Steroids, opiates, benzodiazepines, and polypharmacy can cause delirium.

	delirium.
Endocrine disorders	Hypo- and hyperthyroidism, hypo- and hyperparathyroidism, Addison's disease, and Cushing's disease may cause psychosis.
Intoxication	Amphetamines, cocaine, phencyclidine (PCP, angel dust), methylenedioxypyrovalerone (bath salts), hallucinogens (e.g., lysergic acid diethylamide [LSD], mescaline, psilocybin), dextromethorphan at high doses, and cannabis can trigger psychotic symptoms.
HIV, AIDS	HIV-associated psychosis can occur directly from the viral infection and typically involves a sudden onset (no prodrome), delusions (87% of patients), hallucinations (61% of patients), and mood symptoms (81% of patients).
Other infections	Patients with syphilis, tuberculosis, or other central nervous system infections may develop psychotic symptoms.
Limbic encephalitis	Limbic encephalitis is subacute and involves short-term memory loss, psychosis, behavior changes, and seizures involving the medial temporal lobes and the amygdalae.
Mitochondrial disorders	Mitochondrial disorders usually involve multiple organ systems, so a past medical history of multiple medical problems affecting several organs is often suggestive.