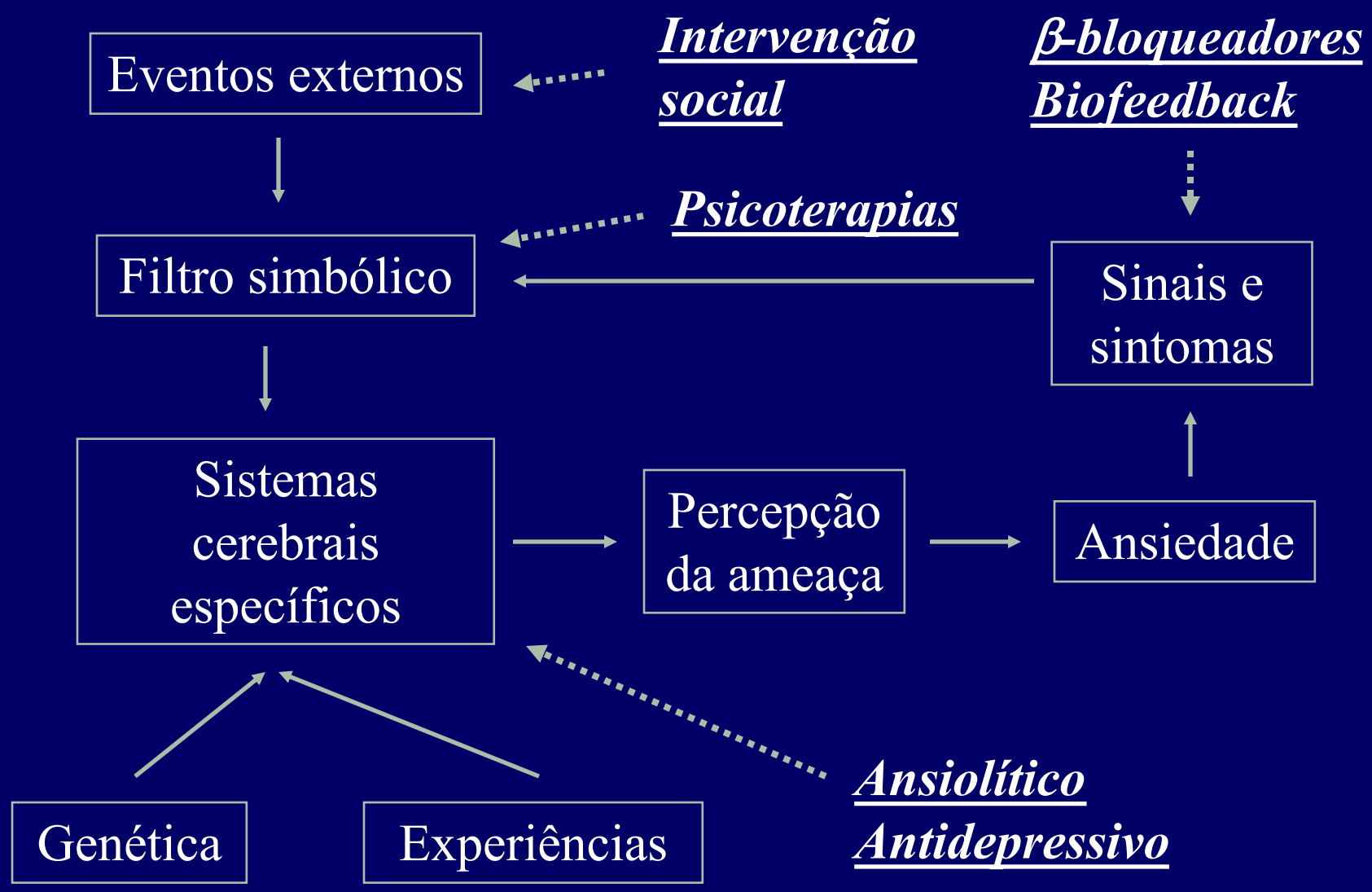
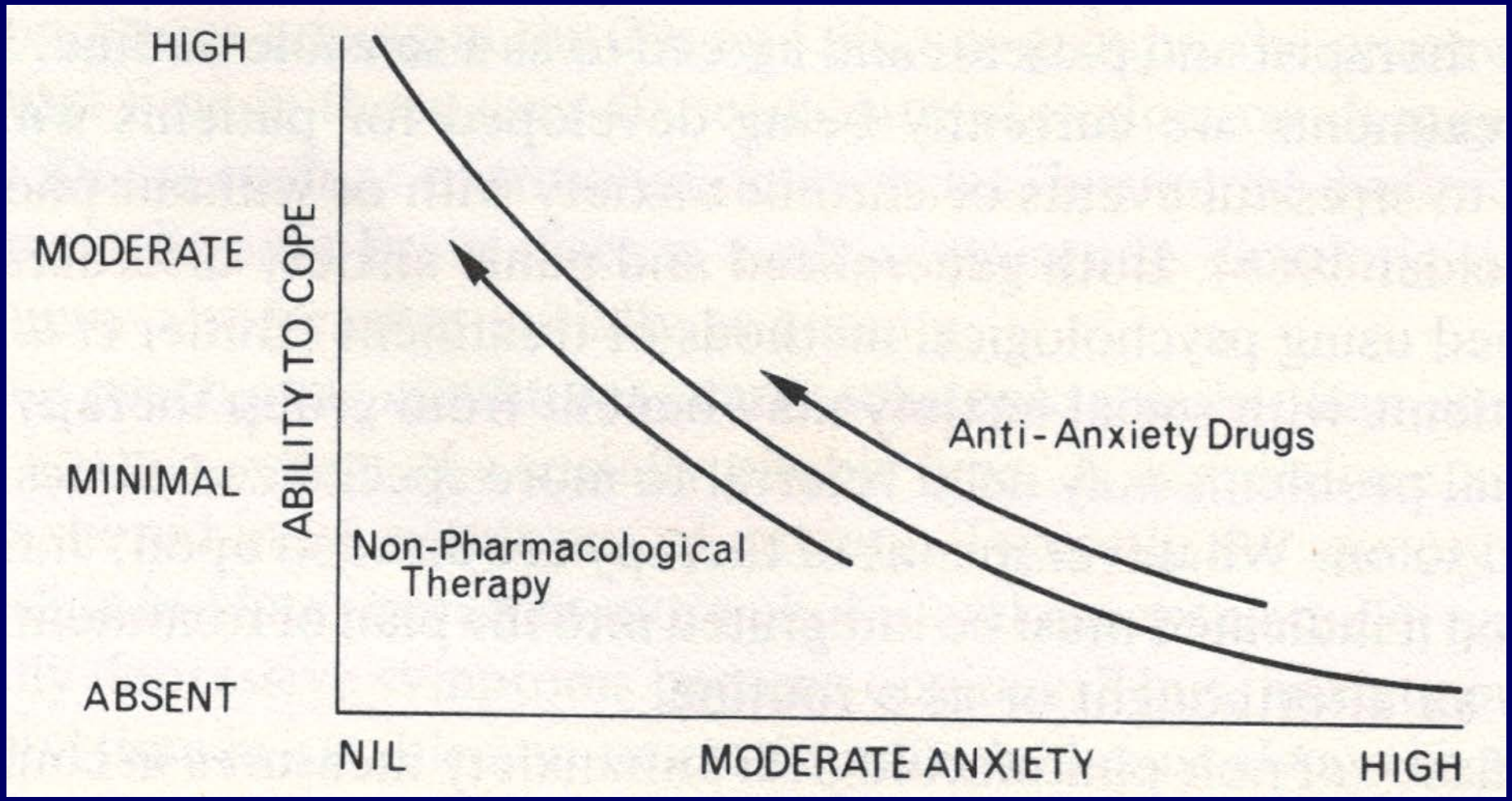
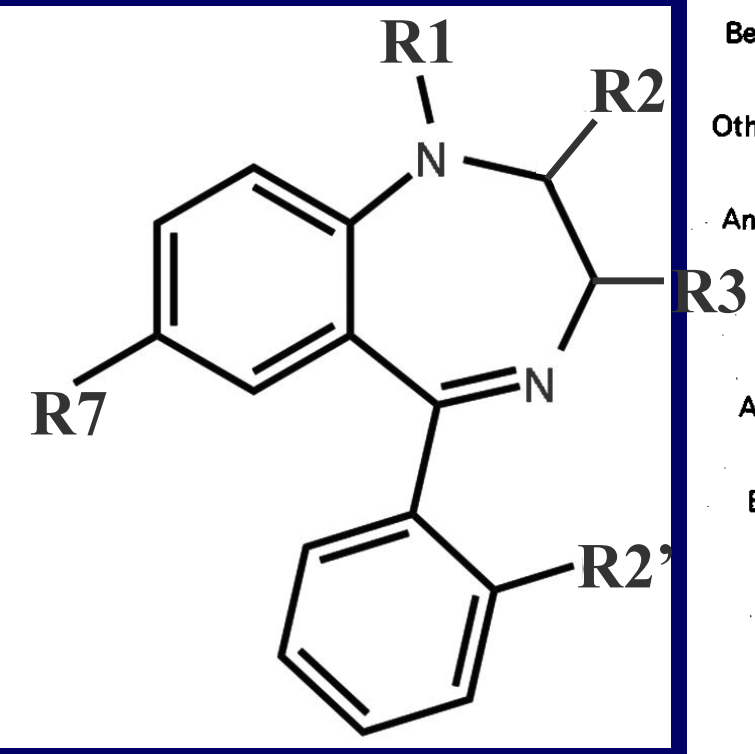

Eventos externos
Intervenção social
β-bloqueadores
Biofeedback
Psicoterapias
Filtro simbólico
Sinais e sintomas
Sistemas cerebrais específicos
Percepção da ameaça
Ansiedade
Genética
Experiências
Ansiolítico
Antidepressivo

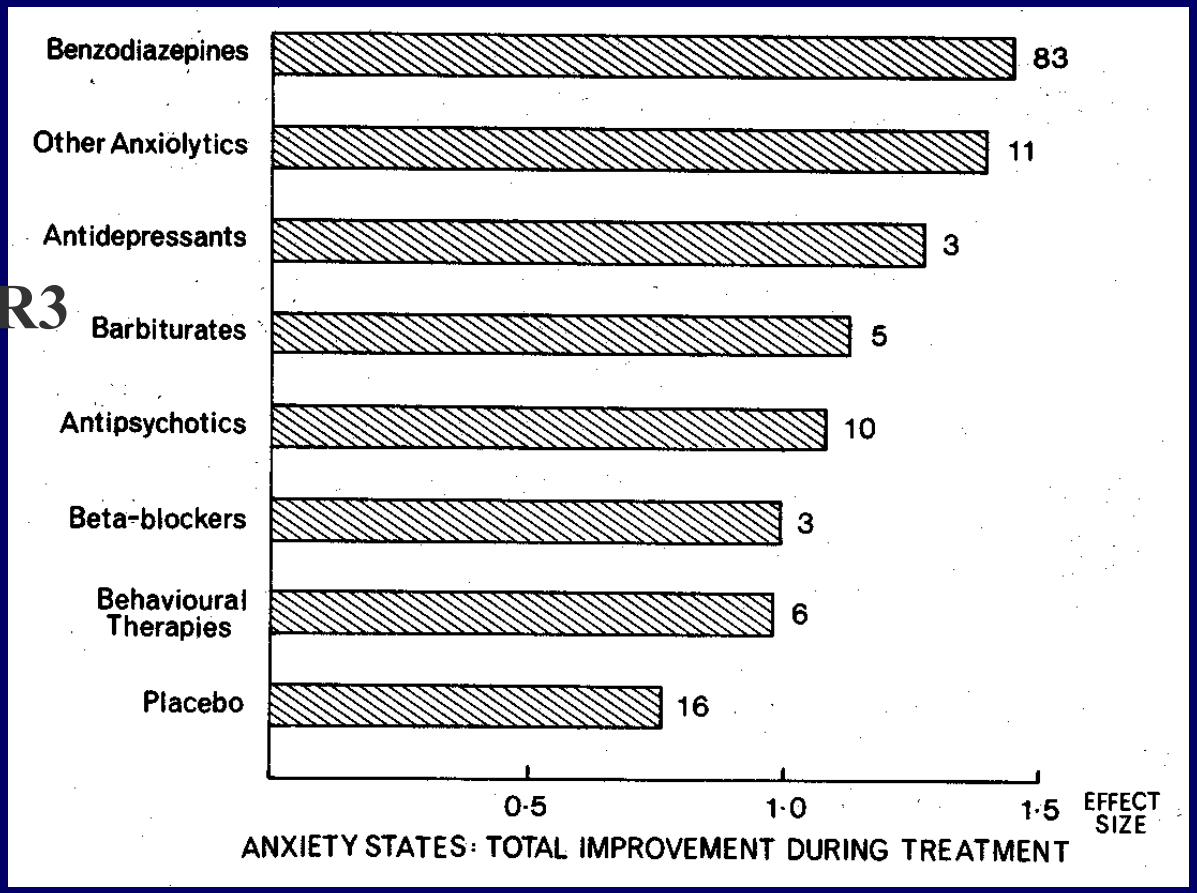
Lader 1990



Quando tratar farmacologicamente a ansiedade?

Eficácia de BZD em ansiedade generalizada





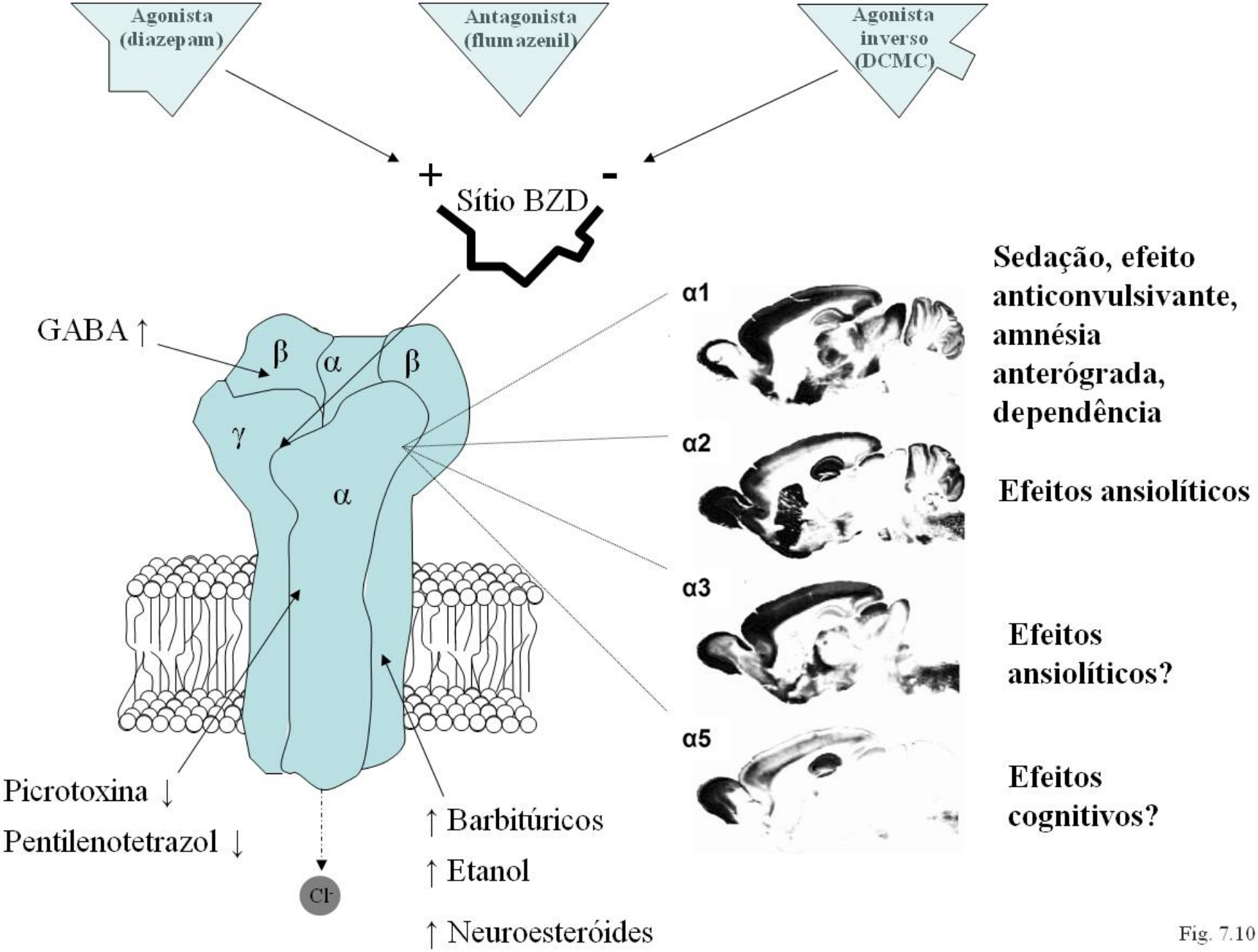
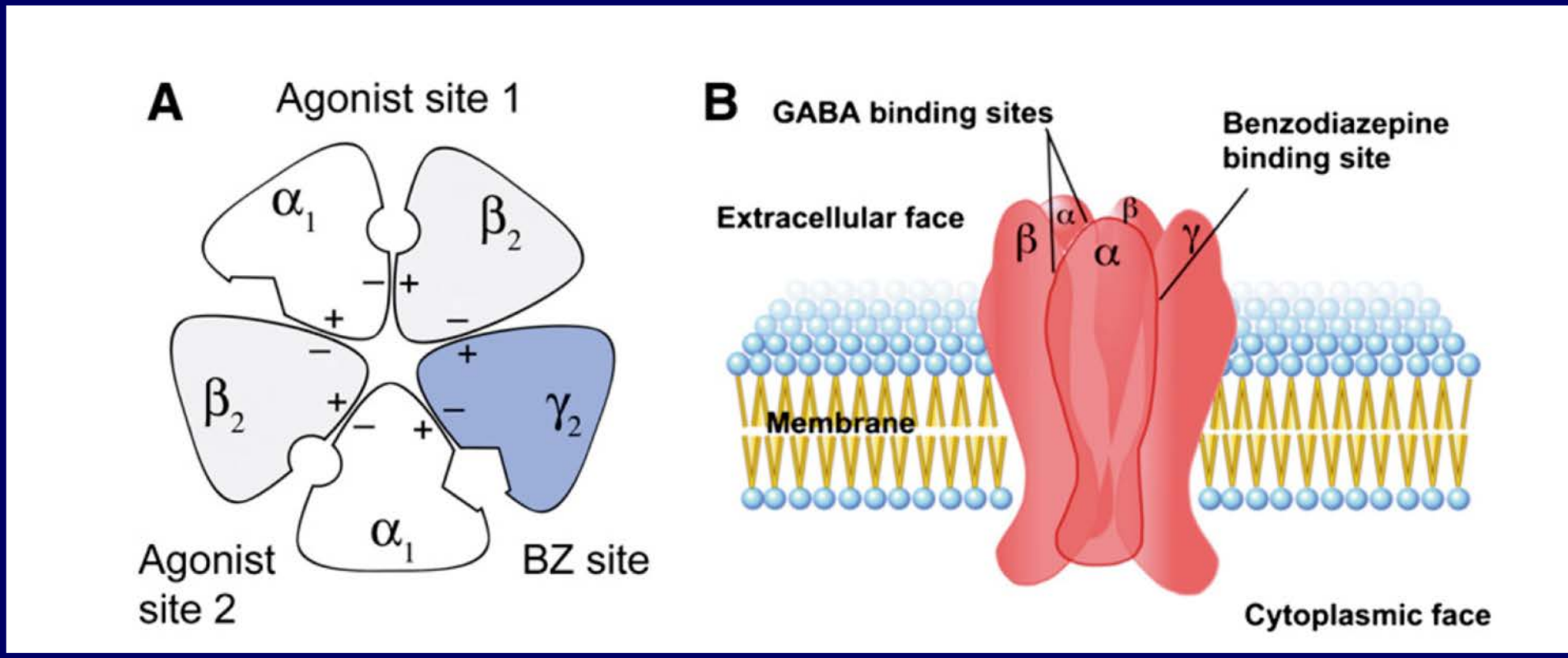

Agonista (diazepam)
Antagonista (flumazenil)
Agonista inverso (DCMC)
+
-
Sítio BZD
GABA ↑
β
α
β
γ
α
Cl-
Picrotoxina ↓
Pentilenotetrazol ↓
↑ Barbitúricos
↑ Etanol
↑ Neuroesteróides
α1
α2
α3
α5
Sedação, efeito anticonvulsivante, amnésia anterógrada, dependência
Efeitos ansiolíticos
Efeitos ansiolíticos?
Efeitos cognitivos?

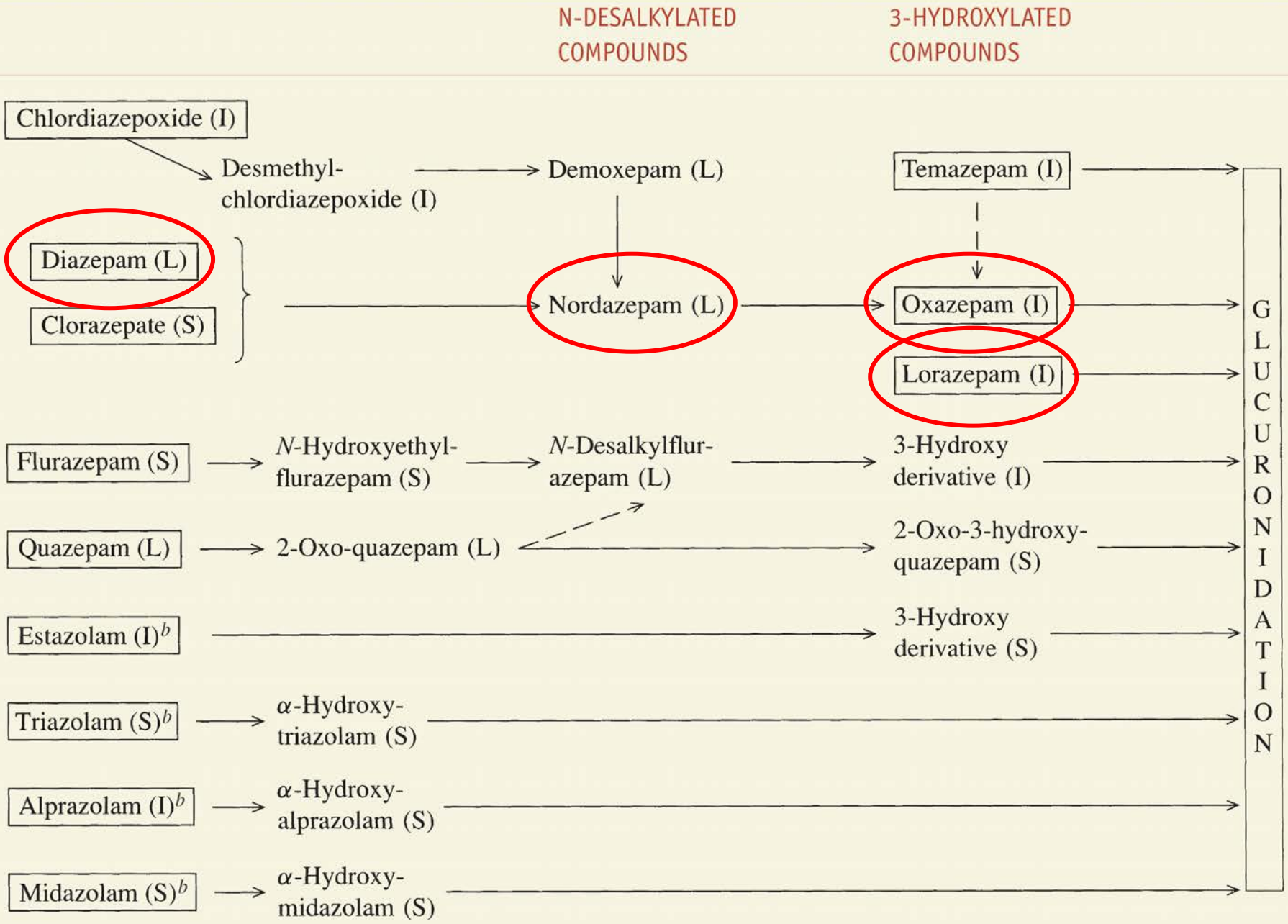
Fig. 7.10

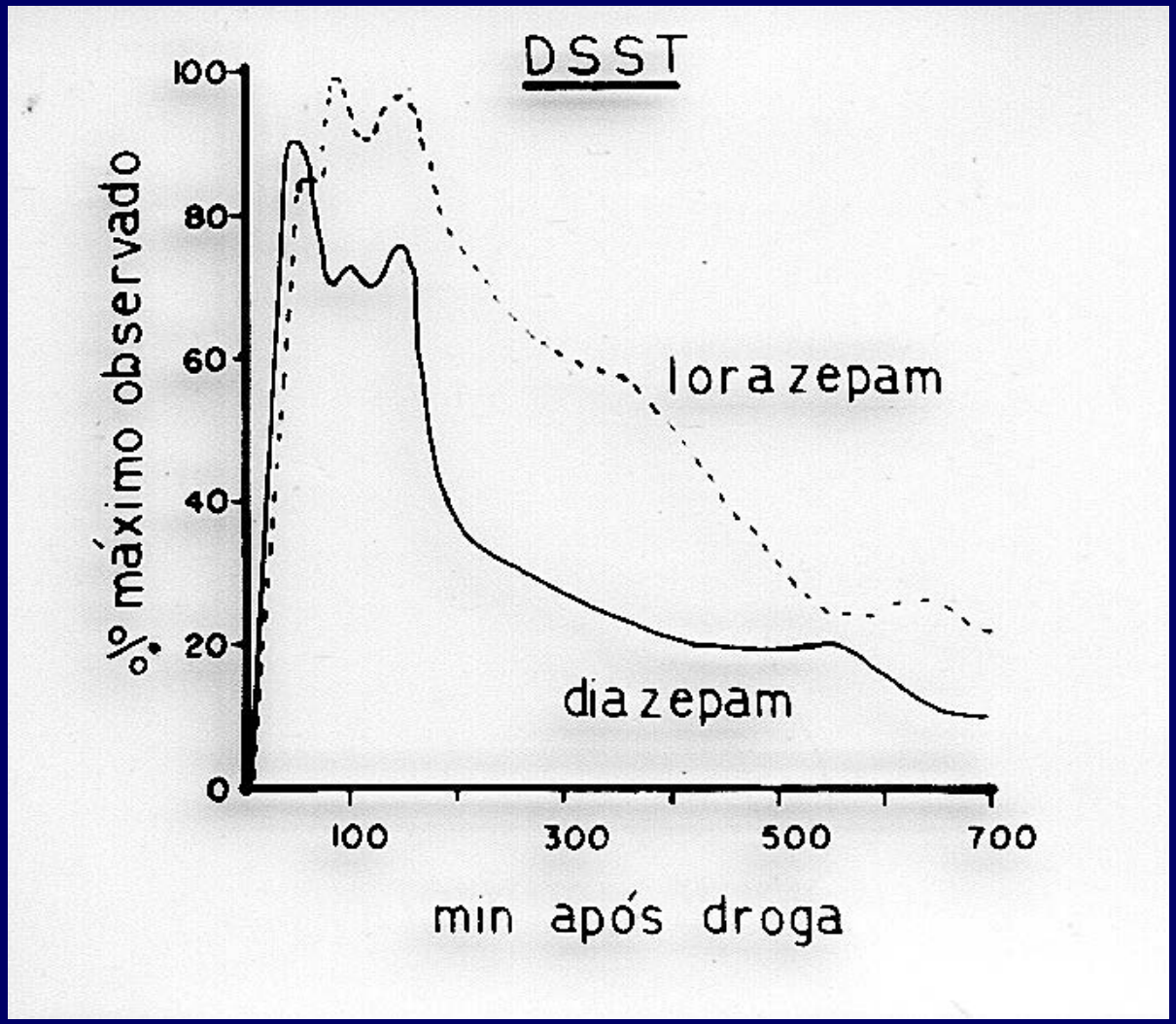
Sítios de ligação dos benzodiazepínicos no receptor GABA-A



Farb & Ratner Pharmacol Rev 2014

Major Metabolic Relationships among Some of the Benzodiazepines[a]



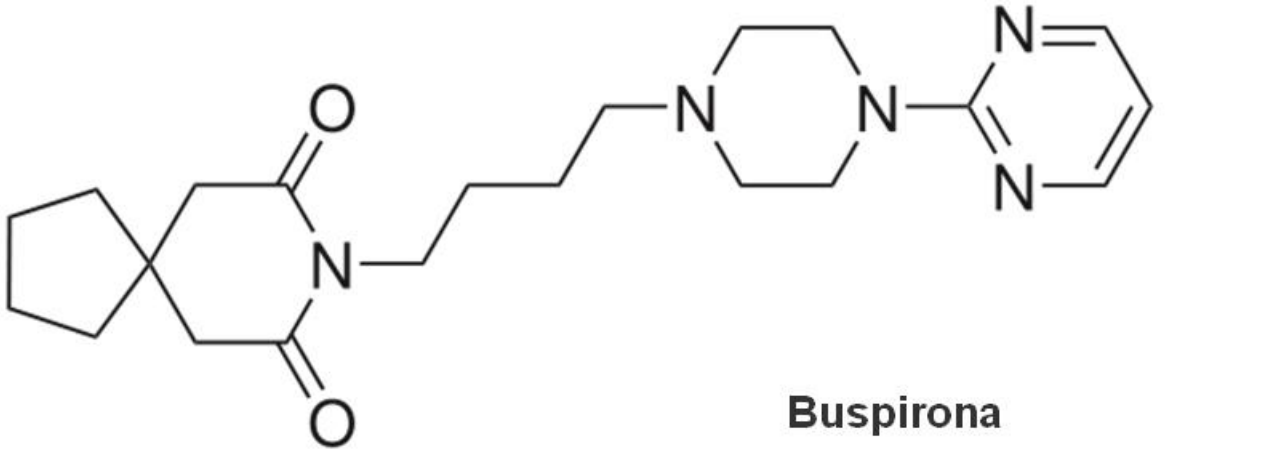


Efeito de prejuízo psicomotor causado por diazepam e lorazepam

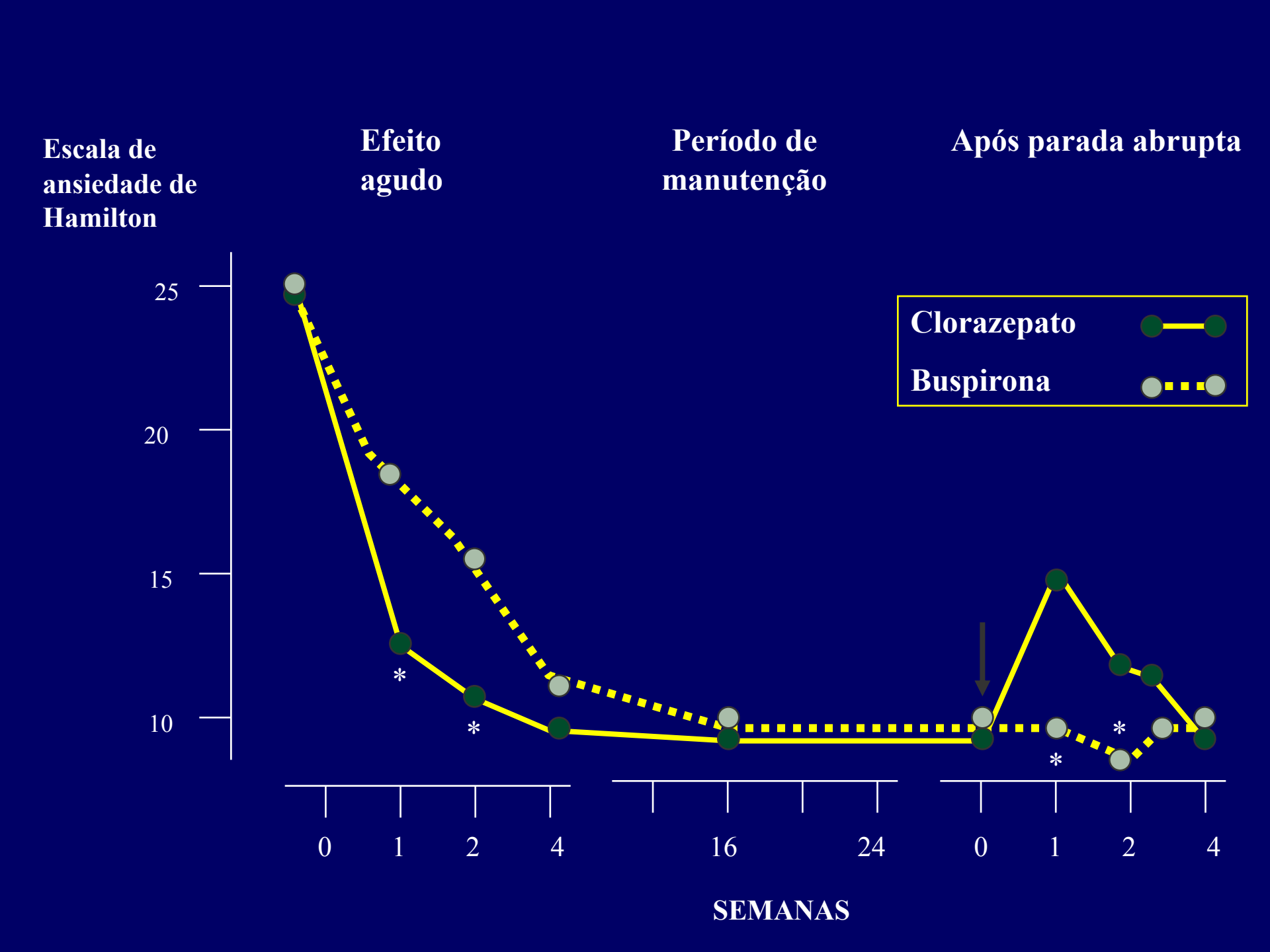
Efeitos dos benzodiazepínicos

Ansiolíticos **Hipnóticos** **Anticonvulsivantes**

Outros: relaxamento muscular central, amnésia anterógrada, tolerância, <u>dependência</u>, <u>prejuízo psicomotor</u>, <u>interação com depressores SNC (ex. etanol)</u>



Buspirona

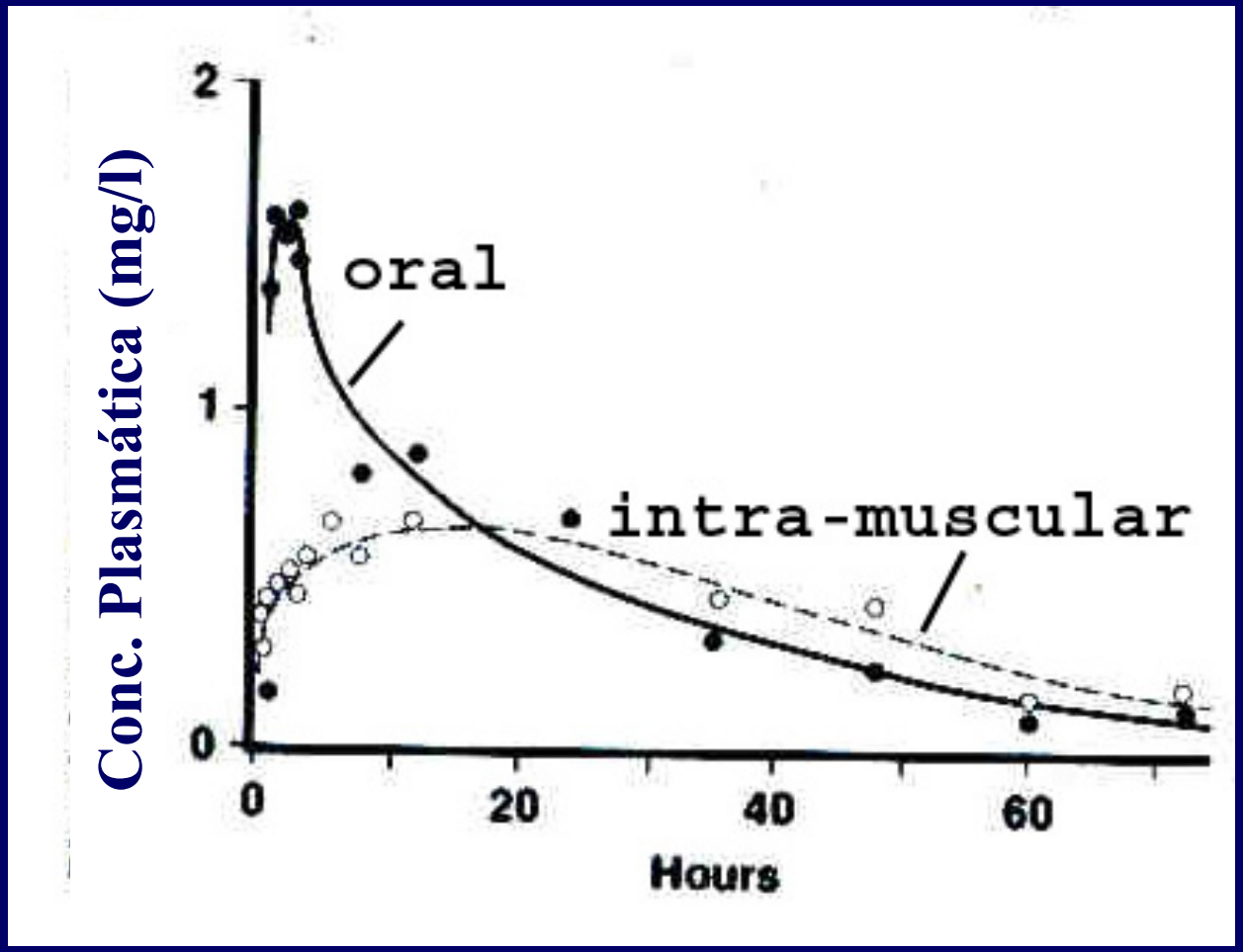

Escala de ansiedade de Hamilton
Efeito agudo
Período de manutenção
Após parada abrupta
25
20
15
10
Clorazepato
Buspirona
*
*
*
*
0
1
2
4
16
24
0
1
2
4
SEMANAS

Transtornos associados à ansiedade: tratamentos de escolha

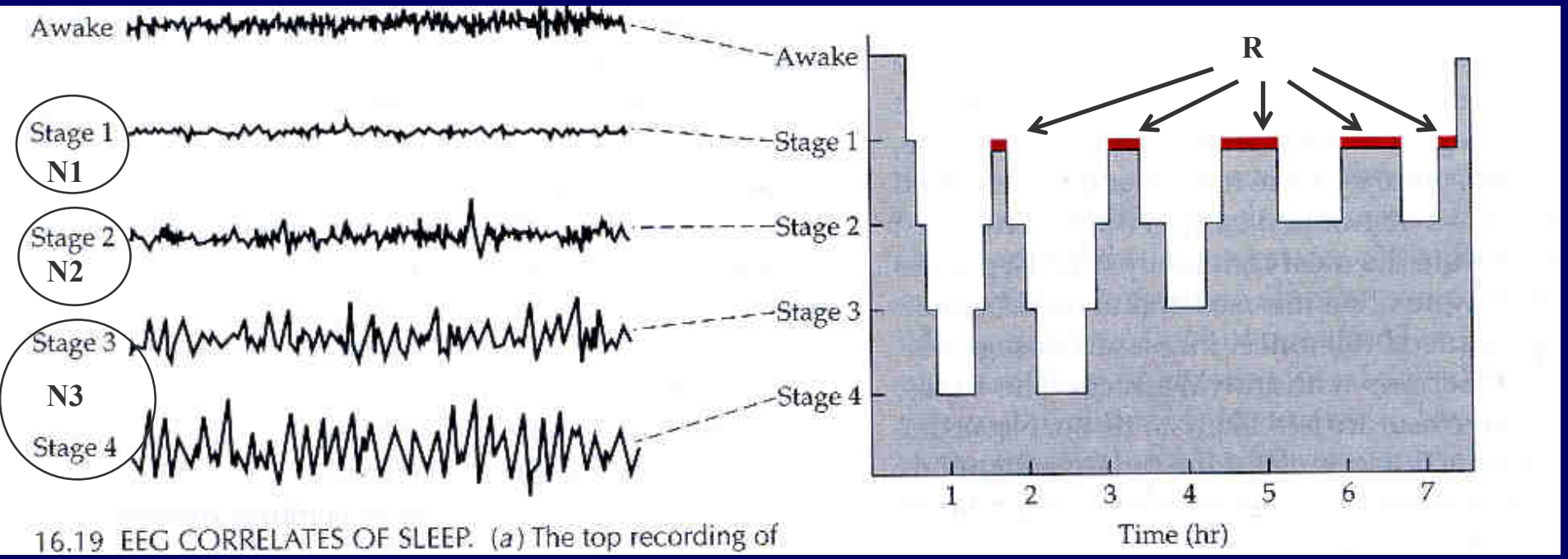
- **Ansiedade generalizada** — **BZD, Buspirona, ISRS**
- **Pânico** — **ISRS**
- **T. obsessivo-compulsivo** — **ISRS**
- **Estresse pós-traumático** — **ISRS**
- **Estresse agudo** — **?**
- **Fobia simples** — **-**
- **Ansiedade (fobia) social** — **ISRS**
- **Agorafobia sem T. de pânico** — **ISRS**
- **Ansiedade devido a condição médica geral** — **?**
- **Ansiedade induzido por substâncias químicas** — **?**
- **Ansiedade atípica** — **?**

ISRS: inbibidores seletivos de receptação de serotonina

Administração de diazepam oral vs. Intra-muscular



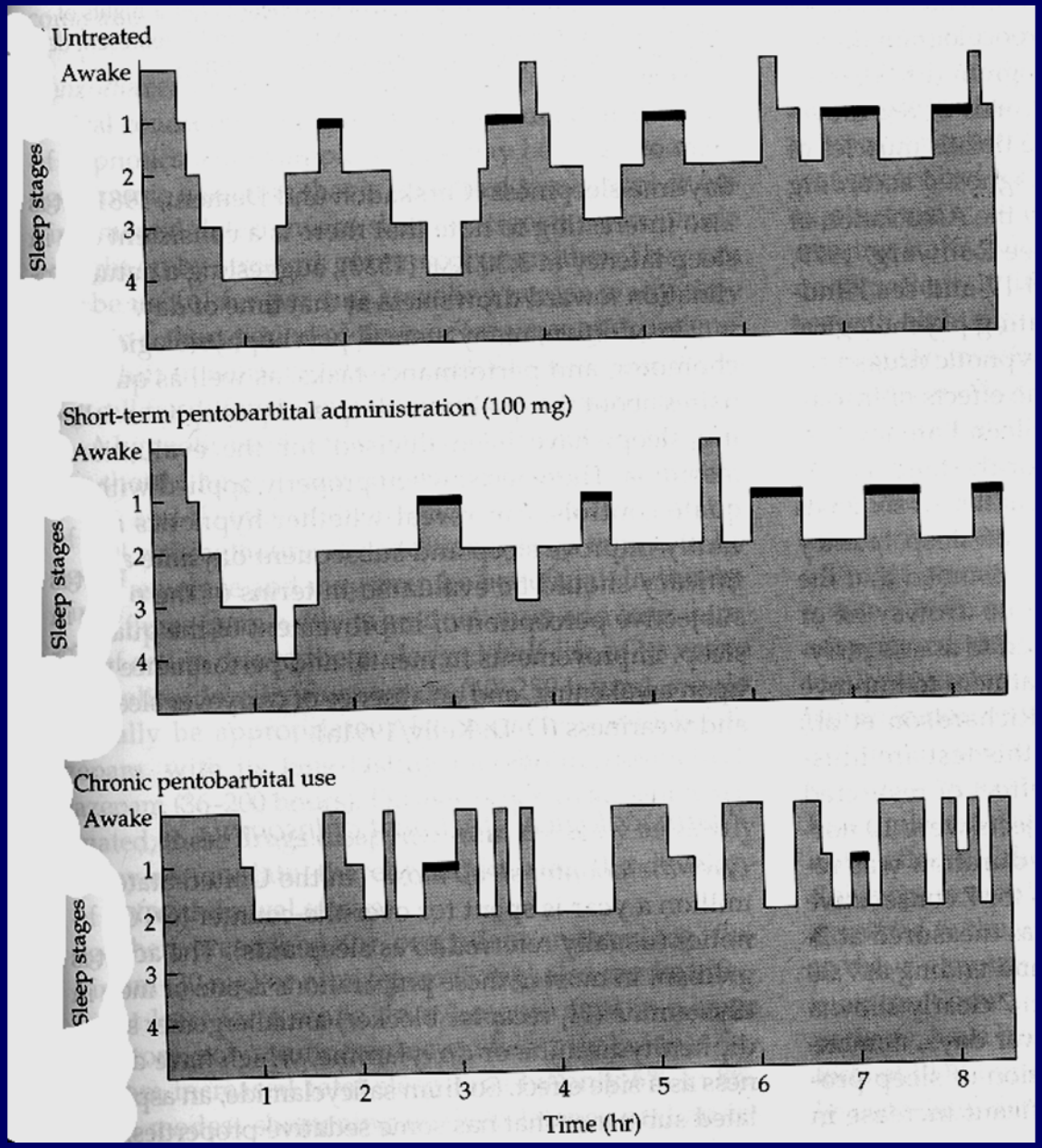
Sono “normal”



16.19 EEG CORRELATES OF SLEEP. (*a*) The top recording of

Tipos de insônia (Lader, 1990)

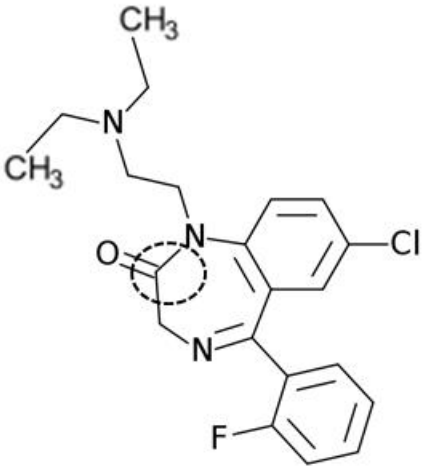
	Tratamento
1. Secundária a problema físico	Problema primário
2. Secundária a problema psiquiátrico	Problema primário
3. Aguda, transitória	Hipnótico
4. Crônica	?



Efeito de barbitúrico no sono

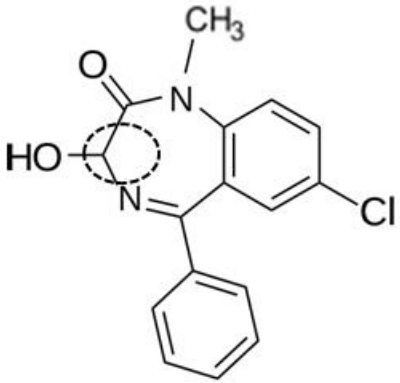
Hipnóticos benzodiazepínicos

2-ceto



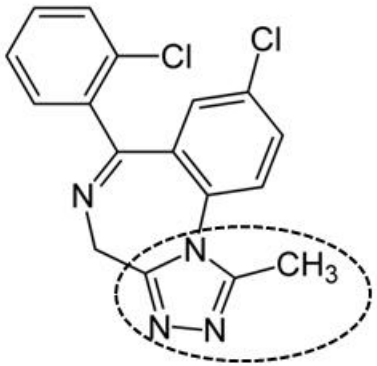
Flurazepam

3-hidróxi



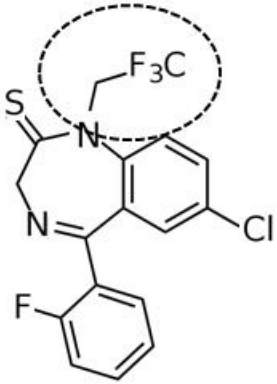
Temazepam

Triazolo



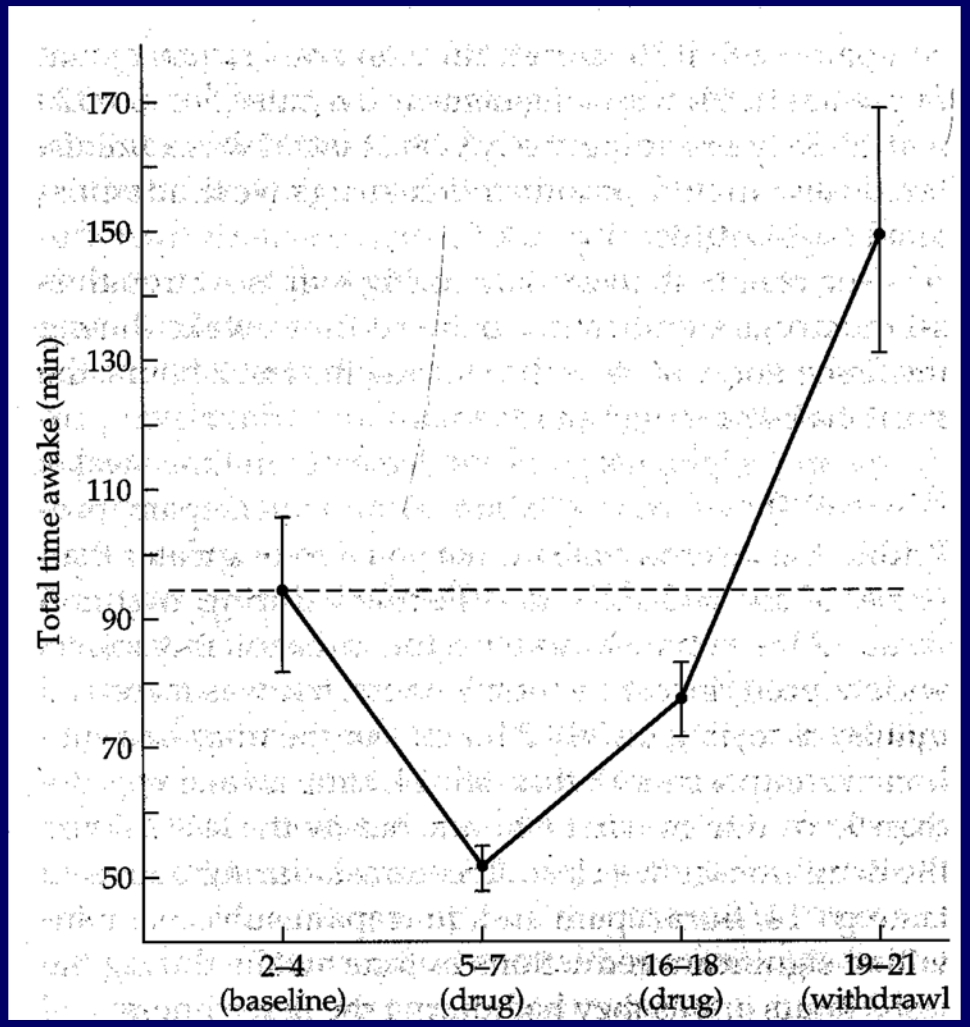
Triazolam

Trifluoretil



Quazepam

Efeito do triazolam no sono



↓ latência
↑ estágio N2
↑ eficiência do sono
↓ sono ondas lentas (N2)
↓ sono REM
<u>Tolerância</u>
<u>"Rebote"</u>

Índice de eficiência do sono: tempo em (N1 + N2 + N3 + R)/tempo na cama

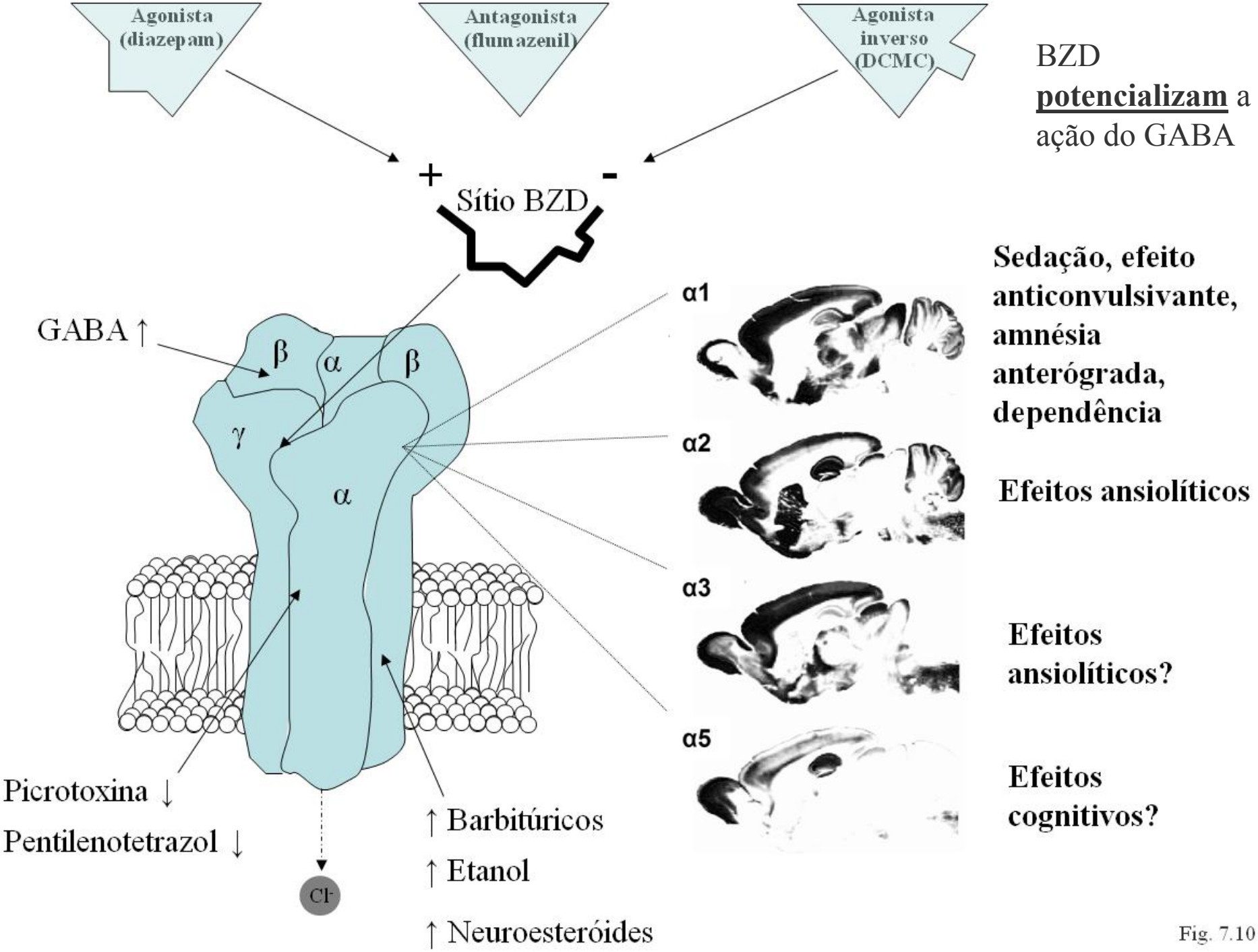
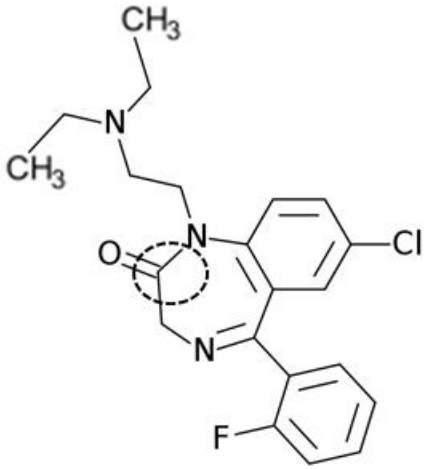

Agonista (diazepam)
Antagonista (flumazenil)
Agonista inverso (DCMC)
BZD **potencializam** a ação do GABA
+
-
Sítio BZD
GABA ↑
β
α
β
γ
α
α1
Sedação, efeito anticonvulsivante, amnésia anterógrada, dependência
α2
Efeitos ansiolíticos
α3
Efeitos ansiolíticos?
α5
Efeitos cognitivos?
Picrotoxina ↓
Pentilenotetrazol ↓
Cl-
↑ Barbitúricos
↑ Etanol
↑ Neuroesteróides

Fig. 7.10

Hipnóticos benzodiazepínicos

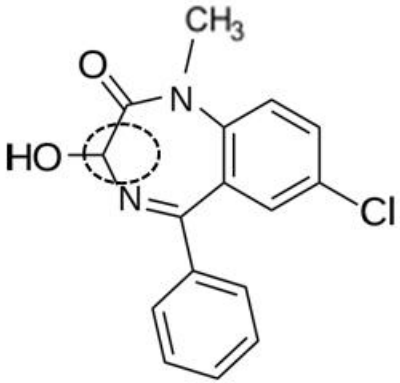
2-ceto



Flurazepam

Longa duração

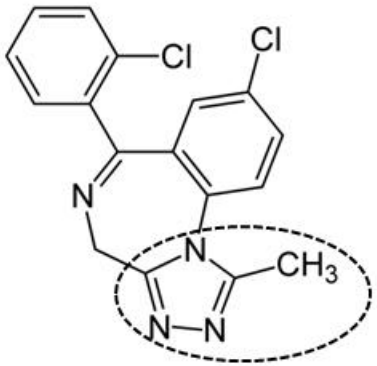
3-hidróxi



Temazepam

Média duração

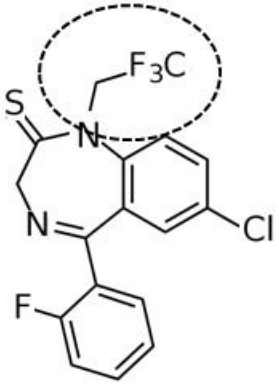
Triazolo



Triazolam

Curta duração

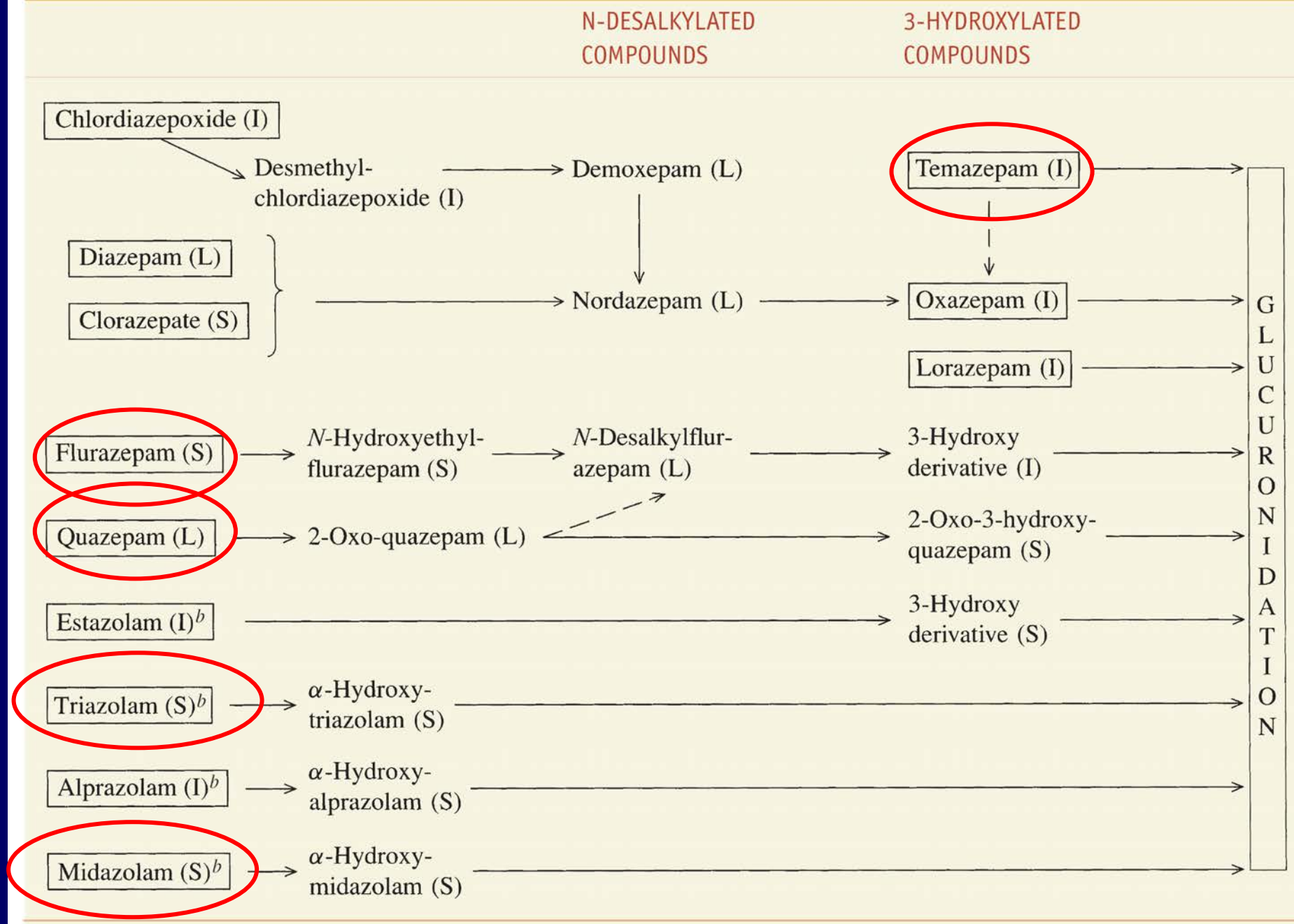
Trifluoretil



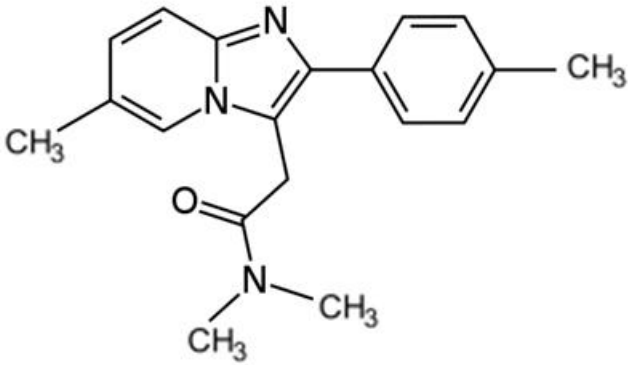
Quazepam

Longa duração

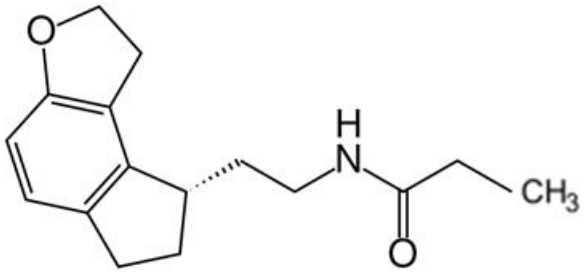
Major Metabolic Relationships among Some of the Benzodiazepines[a]



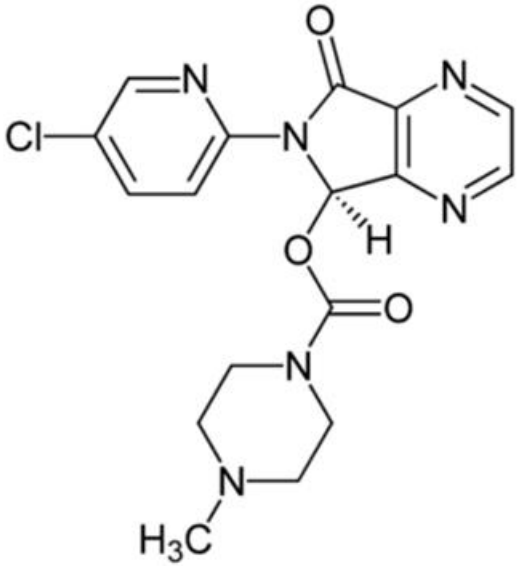
Hipnóticos não-benzodiazepínicos



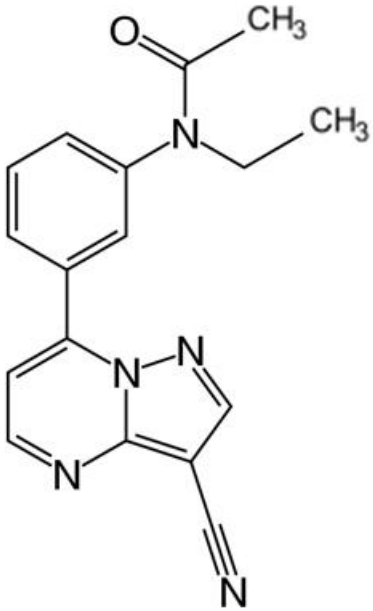
Zolpidem



Ramelteon



Zopiclona

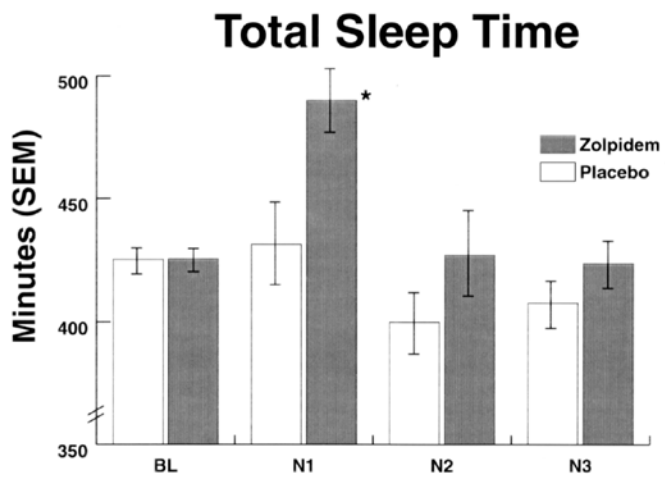


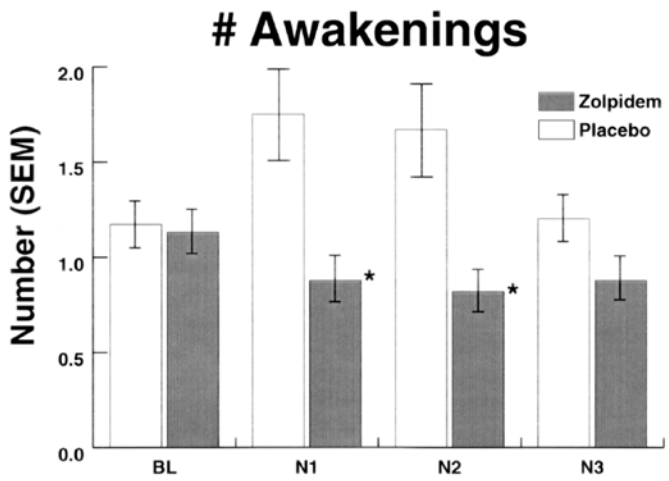
Zaleplona

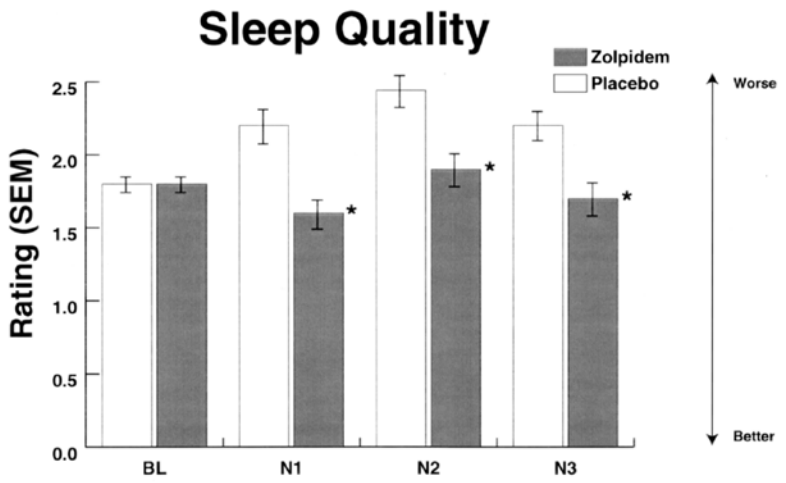
Zolpidem reduces the sleep disturbance of jet lag

Andrew O. Jamieson[a,*], Gary K. Zammit[b], Richard S. Rosenberg[c], Jeffrey R. Davis[d], James K. Walsh[e]

Sleep Med 2001







Zolpidem 10mg nas primeiras 3 noites após viajar de 5-9 zonas the horário

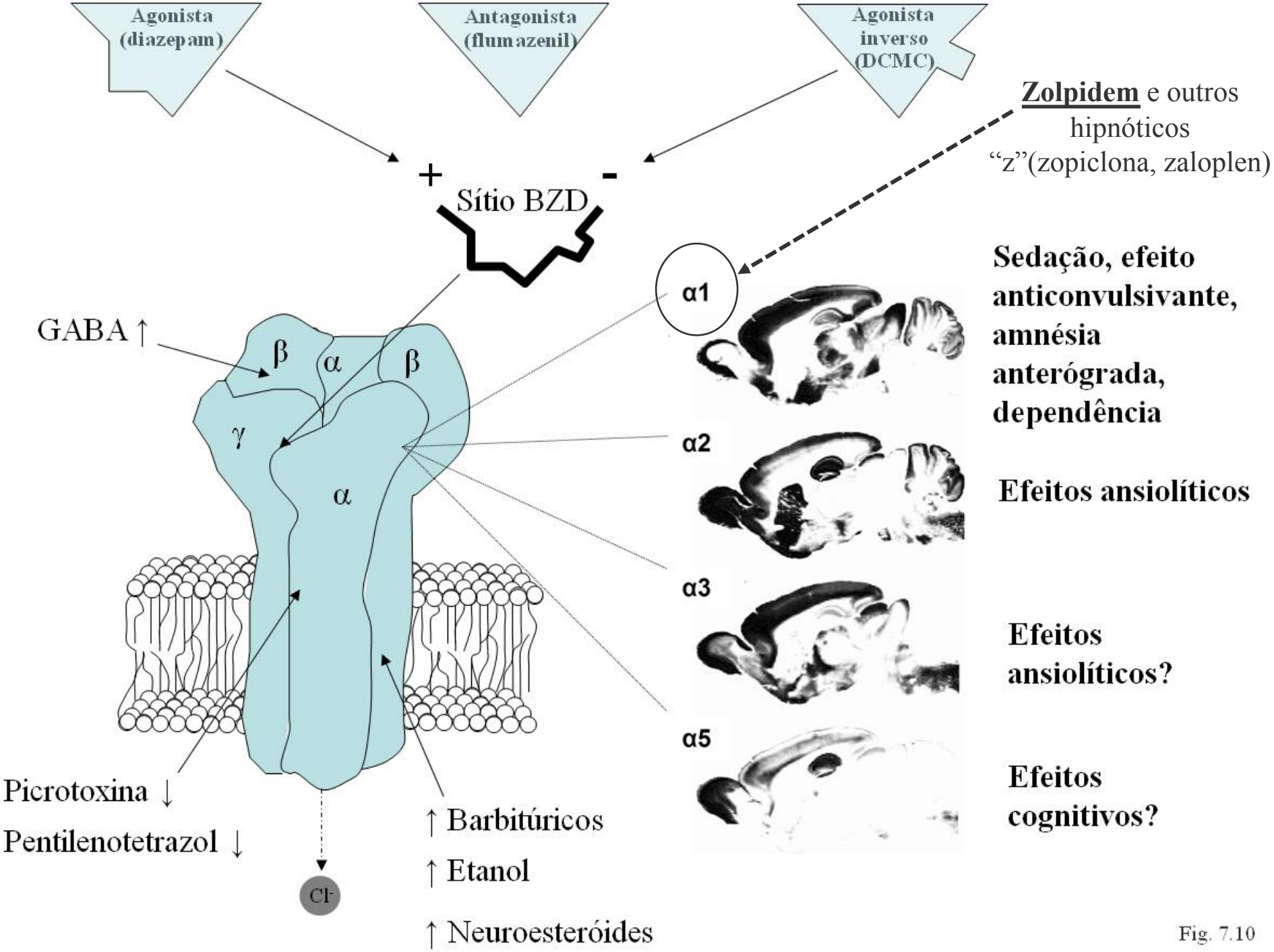

Agonista (diazepam)
Antagonista (flumazenil)
Agonista inverso (DCMC)
Zolpidem e outros hipnóticos "z"(zopiclona, zaloplen)
+
-
Sítio BZD
GABA ↑
β
α
β
γ
α
α1
α2
α3
α5
Sedação, efeito anticonvulsivante, amnésia anterógrada, dependência
Efeitos ansiolíticos
Efeitos ansiolíticos?
Efeitos cognitivos?
Picrotoxina ↓
Pentilenotetrazol ↓
Cl-
↑ Barbitúricos
↑ Etanol
↑ Neuroesteróides

Fig. 7.10

Efeitos de hipnóticos Z sobre o sono

↓ latência
↑ estágio N2 e eficiência do sono
Menor interferência sobre sono REM e N3
Menor Tolerância e "Rebote" do que BZDs

TABLE 2
Summary of the effects of the different hypnotic drugs on the sleep architecture and their potential to induce dependence liability

Drug	Latency to Sleep Onset	Effect on NREM Sleep			Effect on REM Sleep	Sleep Efficiency	Dependence Liability
		Stage N1	Stage N2	Stage N3 also referred as SWS			
Benzodiazepines	↓	↓	↑	↓	↓	↑	High
Z-drugs	↓	↔	↑	↔	↔	↑	Moderate
Ramelteon	↓	↔	↑	↓	↔	↑	Low
Tasimelteon	↓	n.a.	n.a.	n.a.	↑	↑	Low
Melatonin prolonged-release	↓	↔	↔	↔	↔	↑	Low
Agomelatine	↓	↔	↔	↑	↔	↑	Low
Low-dose doxepin	↓	↔	↑	↔	↔	↑	Low
Suvorexant	↓	↔	↑	↔	↑	↑	Low
Trazodone	↔	↔/↓	↔/↓	↔/↑	↔/↓	↔	Low
Amitryptiline	↓	n.a.	n.a	↑	↓	↑	Low
Quetiapine	↓	↔	↑	↔↓	↓	↑	Low
Olanzapine	↓	↔	↔/↑	↑	↓/↔/↑	↑	Low
Gabapentin	↔	↔	↔	↑	↔	↑/↔	Moderate
Pregabalin	↓	↔	↔	↑	↓	↑	Moderate
Mirtazapine	↔	↓	↔	↑	↔	↑	Low

↑: Increase; ↓: decrease; ↔: no change. n.a.: not assessed.

Preços de hipnóticos (2011, para 20 comp.)

Hipnótico		Preço (R$)
Diazepam	(Valium)	10,07
	Genérico	6,32
Flurazepam	Genérico	12,70
Midazolam	(Dormonid)	26,25
	Genérico	17,29
Zolpidem	(Stilnox)	58,03
	Genérico	37,10