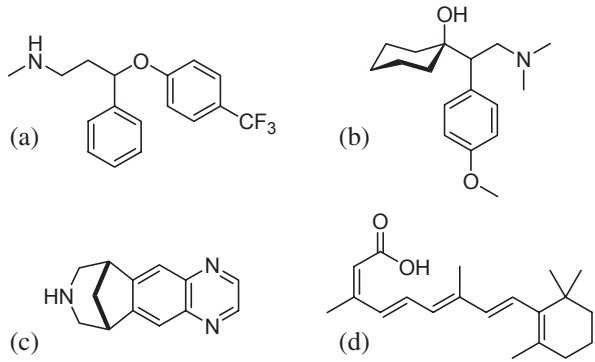

FIGURE 8.21 (a) Prozac® (fluoxetine), (b) Effexor® (venlafaxine), (c) Chantix® (Varenicline), (d) Accutane® (Isotretinoin).

novel pain relievers. An *in vivo* model designed to measure an animal's response to pain would be significantly impacted if a candidate compound is capable of acting as a sedative. Decreased response to pain stimulus might be driven by sedation, rather than an increased threshold to the pain. Understanding the impact of candidate compounds on the CNS can be critical to the success or failure of drug discovery and development programs.

As was the case for cardiovascular safety and toxicology studies, the number of possible targets potentially associated with negative CNS effects is quite extensive. Unless there is significant level of homology between the therapeutic target of interest and a potential CNS "antitargets," most companies do not have the resources to maintain *in vitro* screening systems for the wide range biomolecules that can impact CNS function (Exemplary CNS targets are listed in Table 8.3). Typically, advanced compounds are screened

TABLE 8.3 Exemplary Central Nervous System Targets

Adenosine receptor A2a	Nicotinic acetylcholine receptor
α-adrenergic receptor	NMDA receptor
β-2 adrenergic receptor	Norepinephrine transporter
Cannabinoid receptor 1	Opioid receptor
Dopamine receptor	Serotonin receptor
GABA receptor	Serotonin transporter
Histamine H1 receptor	Substance-P receptor
Monoamine oxidase A	Voltage-gated sodium channel
Muscarinic acetylcholine receptor	Voltage-gated potassium channel