NeuroStar TMS Therapy®

Effective. Precise. Safe.

NEUROSTAR®
TMS THERAPY

A proven non-drug treatment for depression

UNMET NEED

Over 350 million people worldwide suffer from depression today.[1] By the year 2030, depression is predicted to become the number one cause of disability.[2]

The STAR*D trial, the largest and longest study ever conducted to evaluate depression medications, demonstrates that as patients move through medication trials:

...the likelihood of achieving remission is limited and declines with each subsequent treatment[3,4,5,6]

...discontinuation rates due to side effects rise very rapidly[3,5]

Millions of depression sufferers are experiencing intolerable side effects from current therapies without receiving adequate benefit;

These Patients Are Looking For Effective Alternatives.

1. World Health Organization. Depression fact sheet No.369. http://www.who.int/mediacentre/factsheets/fs369/en/index.html. Accessed February 27, 2013.
2. Global Burden of Disease Report (2006) Geneva, World Health Organization.
3. Trivedi MH, et al. (2006). Evaluation of Outcomes with Citalopram for Depression Using Measurement-Based Care in STAR*D Implications for Clinical Practice. *Am J Psychiatry* 163(1):28-40.
4. Fava M, et. al. (2006). A Comparison of Mirtazapine and Nortriptyline Following Two Consecutive Failed Medication Treatments for Depressed Outpatients: A Star*D Report. *Am J Psychiatry* 163(7):1161-1172.
5. Rush AJ, et. al. (2006). Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry*; 163(11):1905-1917.
6. McGrath PJ, et al. (2006). Tranylcypromine Versus Venlafaxine Plus Mirtazapine Following Three Failed Antidepressant Medication Trials for Depression: A STAR*D Report." *Am J Psychiatry* 163(9):1531-1541.

Current Practice: The Medication Treadmill

Few treatment options have been studied and approved by the FDA for use in patients who have failed to benefit from initial treatment. The STAR*D Study shows that clinical effectiveness declines and intolerance increases with each treatment failure.

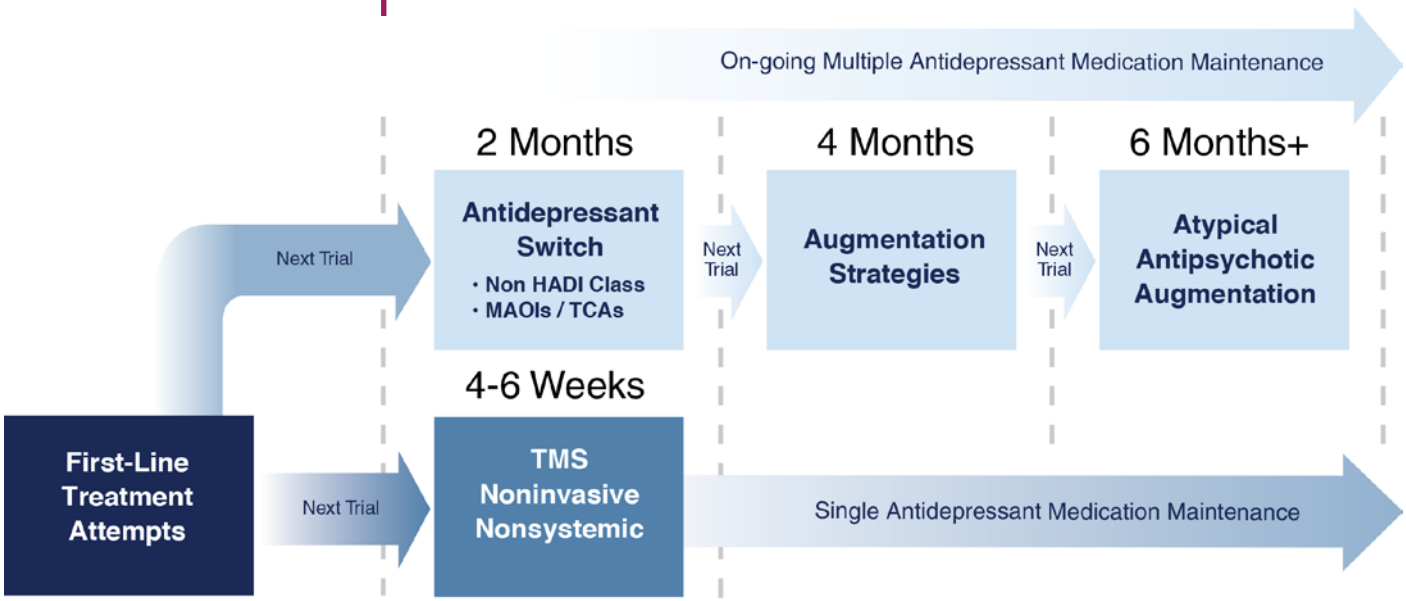
NEUROSTAR® TMS THERAPY

Based on 2010 American Psychiatric Association (APA) Practice Guidelines for Major Depressive Disorder.[1]

PROVEN

Remission for your patients is possible.

NeuroStar TMS Therapy® is a proven effective treatment option for patients who have not benefited from antidepressant medications.



1. American Psychiatric Association (2010) (eds: Gelenberg AJ, Freeman MP, Markowitz JC, Rosenbaum JF, Thase ME, Trivedi MH, Van Rhoads RS). *Practice Guidelines for the Treatment of Patients with Major Depressive Disorder, 3rd Edition*.

Proven Effective Treatment

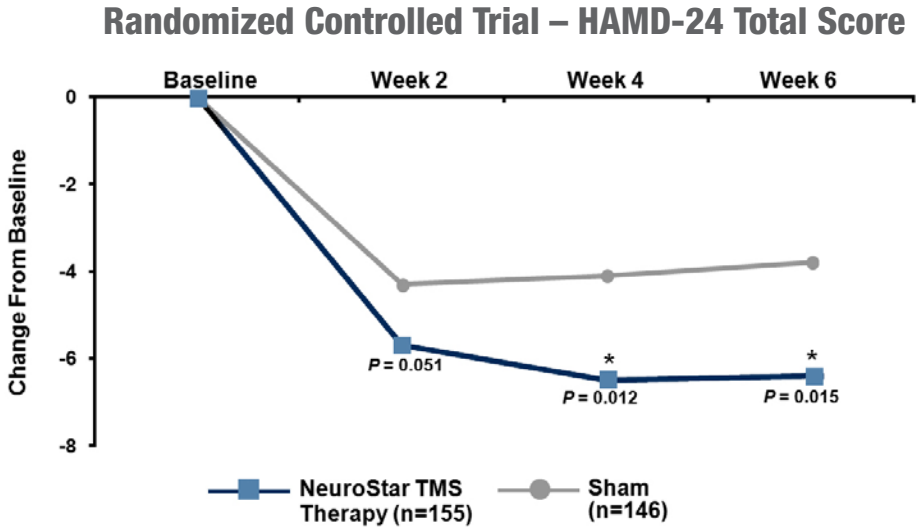
Largest Clinical Data Set of any TMS System in Depression

6 studies completed with over 800 patients

- 2 randomized controlled studies[1,2]
- 2 open-label extensions[3,4]
- 1 open-label post market outcomes study[5]
- 1 open-label long term durability[6]

Robust evidence demonstrates proven efficacy and safety

In a Difficult to Treat Population, there is a Clear Separation Between Active and Sham Treatment[1]



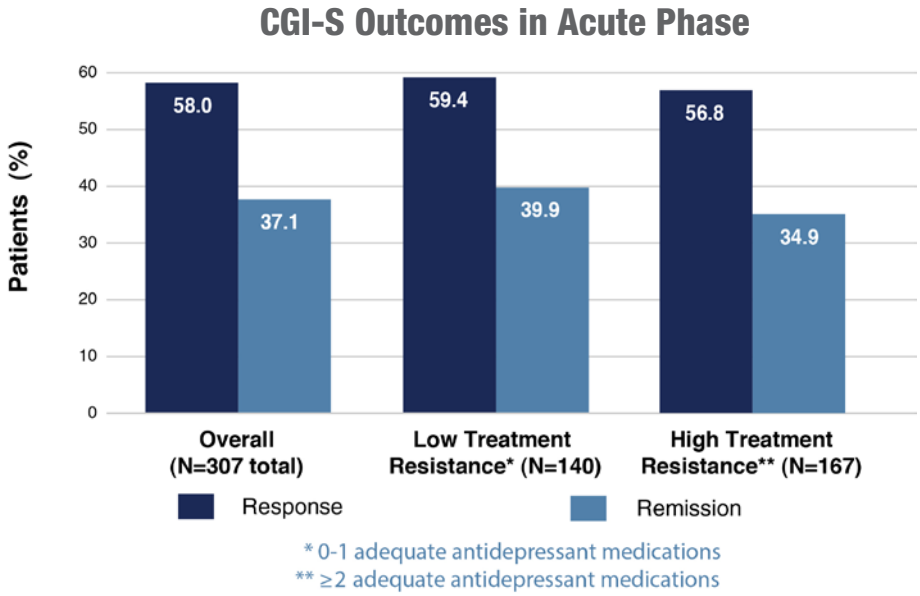
*$P < 0.05$ LOCF, LS mean

Patient Characteristics

- Average number of antidepressant medication trials in current episode = 4 (range: 1 to 23 attempts)
- Majority of treatment attempts were unable to achieve adequate dose and duration of treatment due to intolerance

1. O'Reardon JP, et al. (2007). Efficacy and safety of Transcranial Magnetic Stimulation in the acute treatment of major depression: A multisite randomized controlled trial. *Biol Psychiat* 62(11):1208-1216.
2. George MS, et al. (2010). Daily Left Prefrontal Transcranial Magnetic Stimulation Therapy for Major Depressive Disorder: A Sham-Controlled Randomized Trial. *Arch Gen Psychiat* 67(5):507-516.
3. Avery DH, et al. (2008). Transcranial Magnetic Stimulation in the acute treatment of major depressive disorder: Clinical response in an open-label extension trial. *J Clin Psychiat* 69(3):441-451.
4. McDonald WM, Durkalski V, et al (2011), "Improving the Antidepressant Efficacy of Transcranial Magnetic Stimulation: Maximizing the Number of Stimulations and Treatment Location in Treatment-Resistant Depression. *Depress Anxiety*. Nov; 28(11):973-80.
5. Carpenter LL, et al. (2012). Transcranial Magnetic Stimulation (TMS) for Major Depression: A Multisite, Naturalistic, Observational Study of Acute Treatment Outcomes in Clinical Practice. *Depress Anxiety* 29(7):587–596.
6. Janicak PG, et al. (2010). Durability of clinical benefit with transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant major depression: assessment of relapse during a 6-month, multisite, open-label study. *Brain Stimul* 3(4):187-199.
7. Janicak PG, et al. (2008). Transcranial Magnetic Stimulation in the treatment of major depression: A comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. *J Clin Psychiat* 69(2):222-232.

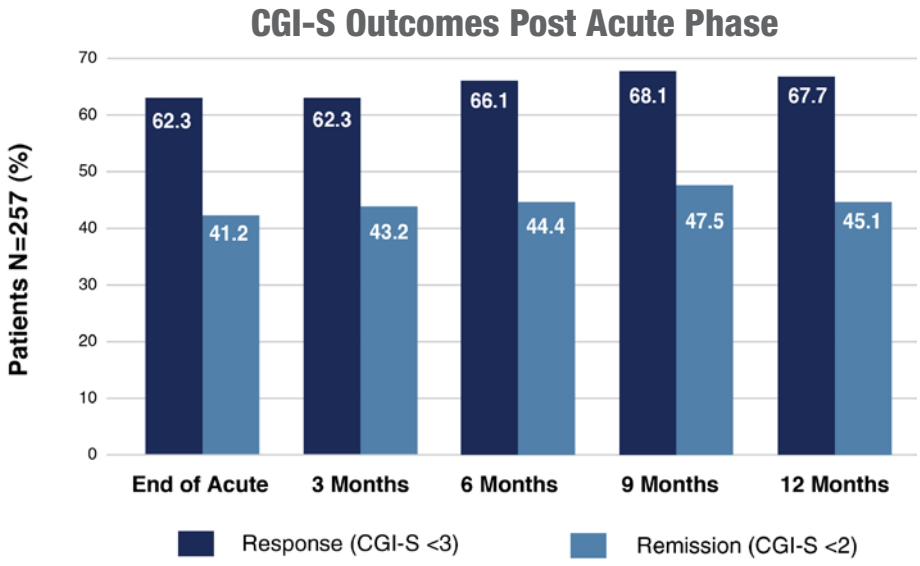
Consistent Response and Remission Rates Across a Broad Range of Treatment Resistance[1]



Patient reported outcomes (PHQ-9) were consistent with physician rated outcomes

42 center trial, mean number of medication treatment attempts in current episode = 3.6

Proven Durability Across 12 Months Post Acute Treatment[2]



PHQ-9 (patient reported outcomes) analysis showed similar results

Outcomes measured for one year following end of acute treatment in open label study

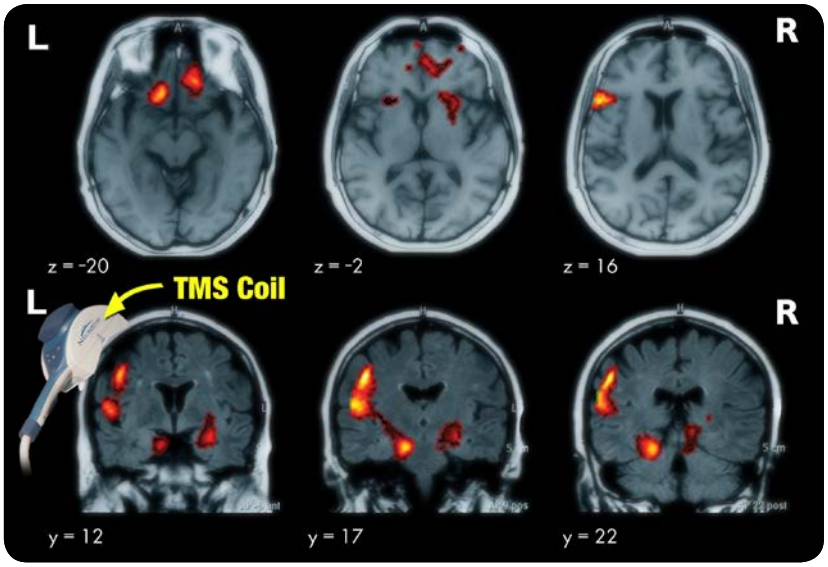
- At 12 months, 68% of study population were responders, 45% were remitters
- Physician directed standard of care
- 36.2% of patients received NeuroStar TMS reintroduction (average of 16 treatments)

1. Carpenter LL, et al. (2012). Transcranial Magnetic Stimulation (TMS) for Major Depression: A Multisite, Naturalistic, Observational Study of Acute Treatment Outcomes in Clinical Practice. *Depress Anxiety* 29(7):587–596.
2. Neuronetics Inc., data on file.

NEUROSTAR®
TMS THERAPY

A Targeted Approach

NeuroStar TMS (Transcranial Magnetic Stimulation) uses a highly focused pulsed magnetic field, similar in type and strength to those produced by a magnetic resonance imaging (MRI) machine, to stimulate cortical neurons.



Neuroimaging studies have documented changes in cortical metabolic activity in tissue directly stimulated by TMS and in distal networks known to be involved in mood regulation[1]

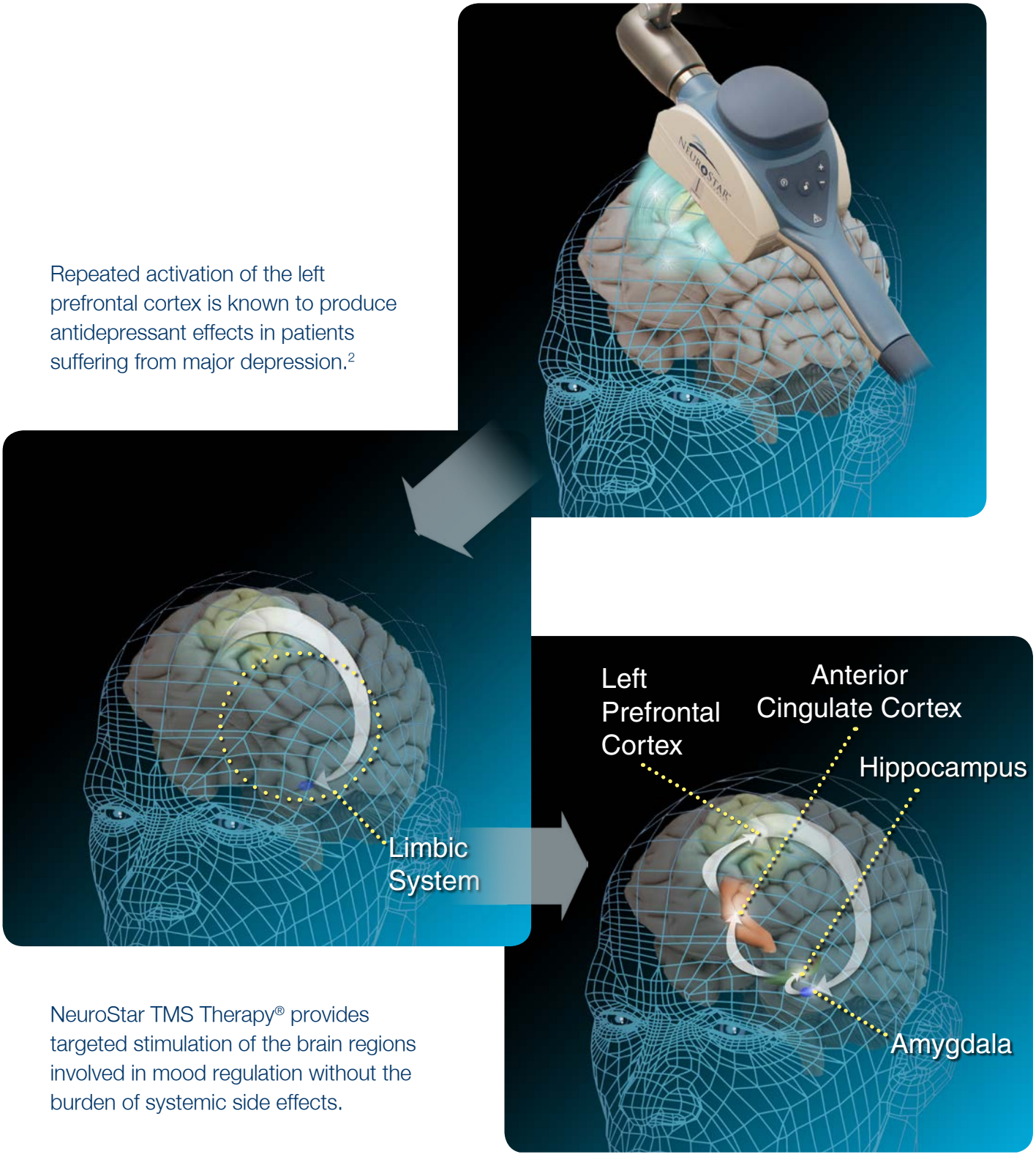
The TMS process

1. Precise pulsed magnetic fields induce small electric currents in the prefrontal cortex of the brain
2. Local neurons depolarize, which leads to activation of deep brain structures via trans-synaptic pathways
3. Activation of these pathways in the limbic system leads to the release of neurotransmitters
4. Blood flow and glucose metabolism rise in the activated regions, which is thought to result in improved mood

1. Kito S, et al. (2008). Changes in Regional Cerebral Blood Flow After Repetitive Transcranial Magnetic Stimulation of the Left Dorsolateral Prefrontal Cortex in Treatment-Resistant Depression. *J Neuropsychiatry Clin Neurosci*. 20(1):74-80.

NeuroStar® Mechanism of Action

Repeated activation of the left prefrontal cortex is known to produce antidepressant effects in patients suffering from major depression.[2]



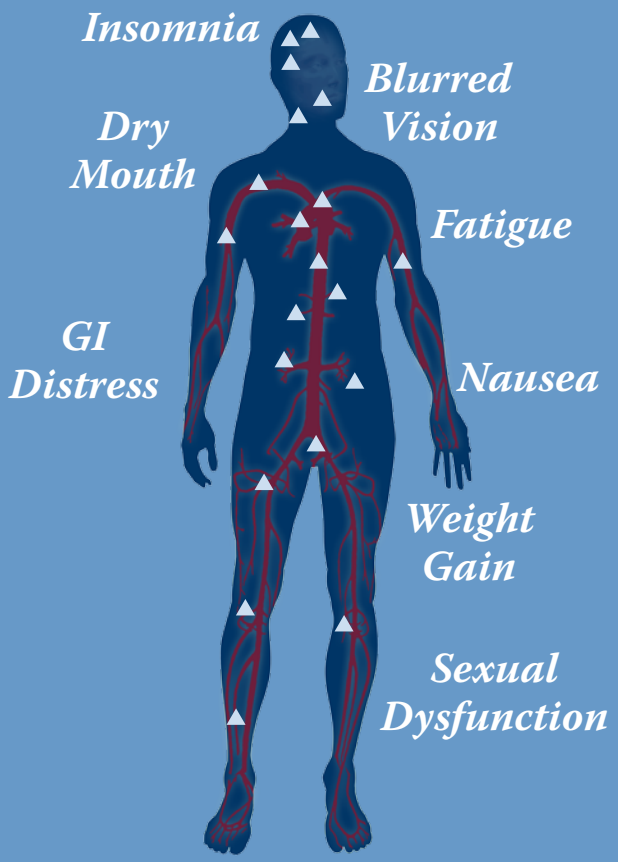
NeuroStar TMS Therapy® provides targeted stimulation of the brain regions involved in mood regulation without the burden of systemic side effects.

The regions known to be involved in mood regulation are the biological targets for TMS

2. Demitrack MA, Thase ME (2009). Clinical Significance of Transcranial Magnetic Stimulation (TMS) in the Treatment of Pharmacoresistant Depression: Synthesis of Recent Data. *Psychopharmacol Bull* 42(2):5-38.

No Systemic Side Effects

DRUG THERAPY



OTHER ADVERSE EVENTS	
Nervousness	Diarrhea
Weakness	Increased Appetite
Abnormal Ejaculation	Dizziness
Constipation	Sweating
Anxiety	Decreased Appetite
Impotence	Tremor
Headache/Migraine	Drowsiness
Decreased Sexual Interest	
Treatment Discontinuation Side Effects	

From product labeling for currently marketed antidepressant medications; adverse events occurring at an incidence >5% incidence and 2x the rate of placebo treatment (Neuronetics, Inc, data on file)

NEUROSTAR® TMS THERAPY

Pain or Discomfort

- The most common side effect is pain or discomfort at or near treatment site

OTHER ADVERSE EVENTS
Eye Pain
Toothache
Muscle Twitching
Facial Pain
Pain of Skin

Adverse events are transient, occur during TMS treatment and do not occur for most patients after the first week of treatment

In clinical trials, fewer than 5% of patients discontinued treatment with NeuroStar TMS Therapy® due to adverse events.

There is a rare risk of seizure associated with TMS treatment (<0.1% per acute treatment course).[1]

1. Janicak PG, et al. (2008). Transcranial Magnetic Stimulation in the treatment of major depression: A comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. *J Clin Psychiatry* 69(2):222-232.