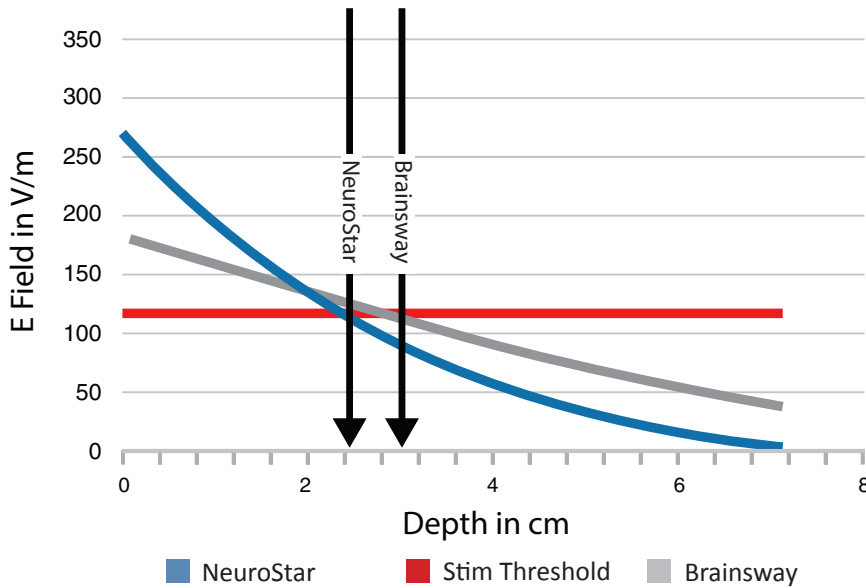


Minimal Difference in Stimulation Depth

NeuroStar vs Brainsway Depth¹

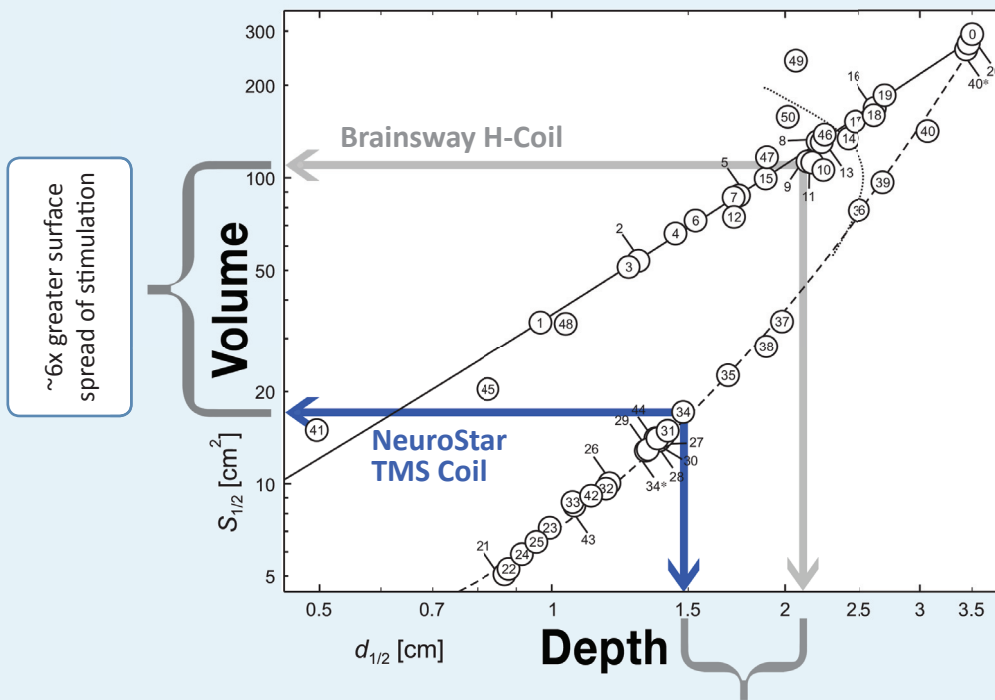


- NeuroStar TMS Therapy[®] uses a targeted, focused approach with precise pulsed magnetic fields
- In publications on TMS stimulation depth, different treatment level settings were assumed by each author which results in depths ranging from 1.5 – 2.5 cm for NeuroStar and 2.0 – 3.0 cm for Brainsway. Regardless of the level settings assumed by each author, each analysis confirms a difference in stimulation depth of only 0.5 cm

No clinically significant difference in stimulation depth between NeuroStar TMS Therapy and dTMS

Neuronetics, Inc. data on file

An Analysis of Coil Designs and Lateral Spread of Stimulation Volume²



- According to a published analysis, marginal deeper electric field penetration of 0.5 cm is achieved at the expense of focality. BrainswayTMS is unfocal (diffuse) which may be associated with increased risk of seizures and other side effects²

The power levels used in this analysis were lower than in a typical TMS treatment

~0.5 cm difference in depth of penetration (data shown is at 100% MT drive level)

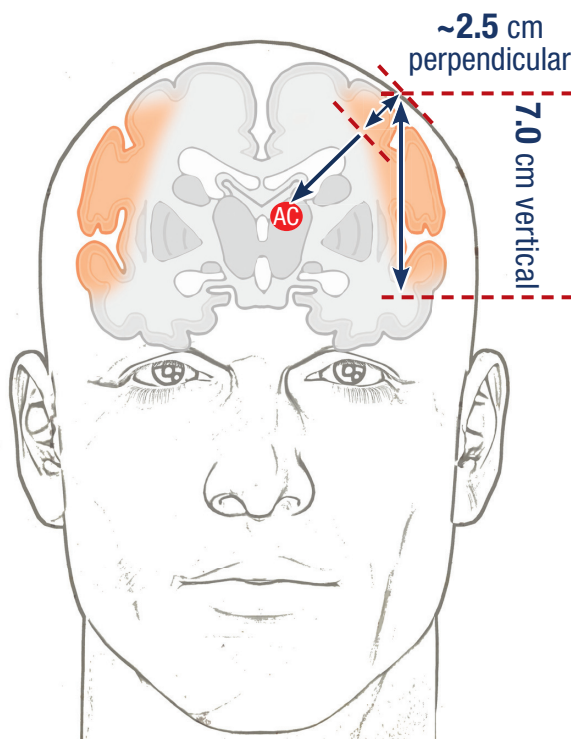
Stimulation Depths with TMS

- NeuroStar TMS field is precise and targeted; while the Brainsway TMS field is diffuse along the curvature of the head like a “cap”
- Both Neurostar TMS and Brainsway directly stimulate the prefrontal cortex, indirectly stimulating the anterior cingulate (AC) and other deep structures related to depression
- The difference in stimulation depth in the direction of the closest depression target, the anterior cingulate (AC), is clinically insignificant (only 0.5 cm)

Understanding the Measurement of TMS Depths

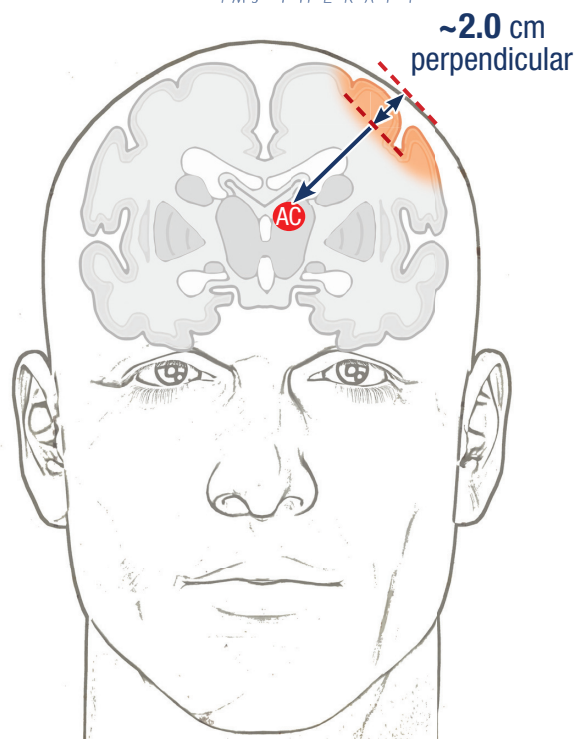
- In a Brainsway analysis, comparison of the stimulation depths between NeuroStar and Brainsway devices is not an accurate comparison³
 - The stimulation depth of the Heschl coil is 6.0 – 7.0 cm and measured **on a vertical line**
 - The stimulation depth of the NeuroStar coil is 2.0 cm and measured **on a perpendicular line**
- The appropriate comparison shows only a **0.5 cm difference** in stimulation depth into the cortex.² Deeper structures associated with mood are only indirectly stimulated by TMS and dTMS devices

Brainsway



Brainsway Depth Toward AC ≈2.5 cm

NEUROSTAR[®] TMS THERAPY



NeuroStar Depth Toward AC ≈2.0 cm

Stimulation Depths with TMS

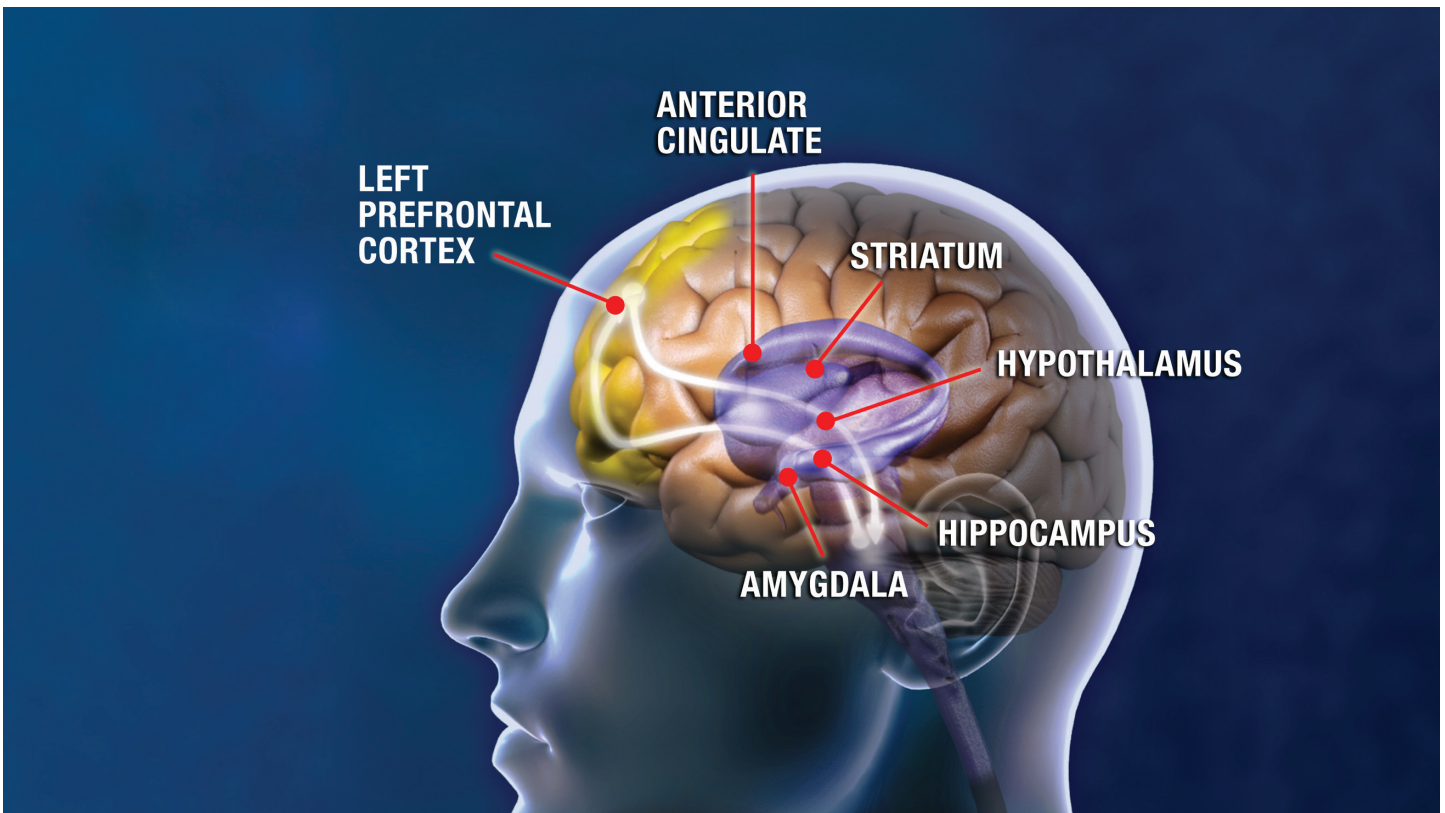
No Difference in Stimulated Depression Targets Between Brainsway and NeuroStar

- All TMS devices directly stimulate the prefrontal cortex and indirectly stimulate deeper brain structures, presumably through neural network connections in the brain⁴
- All depression related targets are stimulated in a similar manner by both Brainsway and NeuroStar TMS devices, with both providing the same level of “deep” stimulation.
- Brainsway TMS device stimulates collateral surface tissue that is unrelated to mood regulation targets

Comparison of the effects of the NeuroStar TMS and Brainsway TMS systems on the brain anatomy

Target Anatomy for Depression Therapy	Shortest Distance from TMS Coil	Does NeuroStar Stimulate?		Does Brainsway Stimulate?	
		Direct	Indirect	Direct	Indirect
Left DLPFC	~1.5 cm	Y	–	Y	–
Anterior Cingulate	~6.0 cm	N	Y	N	Y
Nucleus Accumbens	~7.0 cm	N	Y	N	Y
Amygdala	~8.5 cm	N	Y	N	Y
Striatum	~8.5 cm	N	Y	N	Y
Hypothalamus	~9.0 cm	N	Y	N	Y
Hippocampus	~10.0 cm	N	Y	N	Y

Target Anatomy for Depression Therapy



Summary

- **All TMS is “deep”** by virtue of a similar level of direct stimulation to the left prefrontal cortex and indirect modulation of deep targets via neural pathways
- Brainsway TMS device depth of stimulation is only ~0.5 cm greater than the NeuroStar TMS System which is not clinically meaningful
- Brainsway TMS device does not directly stimulate any depression-related deep brain structures
- Brainsway TMS device does stimulate large volumes of collateral cortex that is not associated with mood regulation
 - Stimulation of collateral cortex may have unanticipated side effects
- NeuroStar TMS Therapy® stimulates key structures of the brain associated with depression as a safe, targeted and effective treatment without stimulating unrelated areas of the brain

References

1. Neuronetics, Inc. data on file.
2. Deng ZD, et al. (2013) Electric field depth-focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs. *Brain Stimul* 6(1):1-13.
3. Roth Y, et al. (2007) Three-Dimensional Distribution of the Electric Field Induced in the Brain by Transcranial Magnetic Stimulation Using Figure-8 and Deep H-Coils. *J Clin Neurophysiol* 24(1):32-8.
4. Kito S, et al. (2008) Regional Cerebral Blood Flow Changes after Low-Frequency Transcranial Magnetic Stimulation of the Right Dorsolateral Prefrontal Cortex in Treatment-Resistant Depression. *Neuropsychobiology* 58(1):29-36.

About NeuroStar TMS Therapy

NeuroStar TMS Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to receive satisfactory improvement from prior antidepressant medication in the current episode.

Most common adverse event related to TMS is localized pain or discomfort at or near the treatment site.

NeuroStar TMS Therapy is contraindicated in patients with non-removable conductive metal in or near the head.

Post-marketing experience confirms a rare risk of seizure with NeuroStar TMS Therapy (<0.1% per patient).¹