



THE UNIVERSITY OF ARIZONA

The Effect of Non-invasive Transcranial Focused Ultrasound Targeting the Default Mode Network on Depression

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Abstract

Background: Up to 50% of individuals fail to respond to current depression treatments (Gaynes et al., 2020). Repetitive negative thought and the default mode network are considered mechanisms of action in the development and maintenance of depression, which can be targeted using transcranial focused ultrasound, a novel neuromodulation technique.

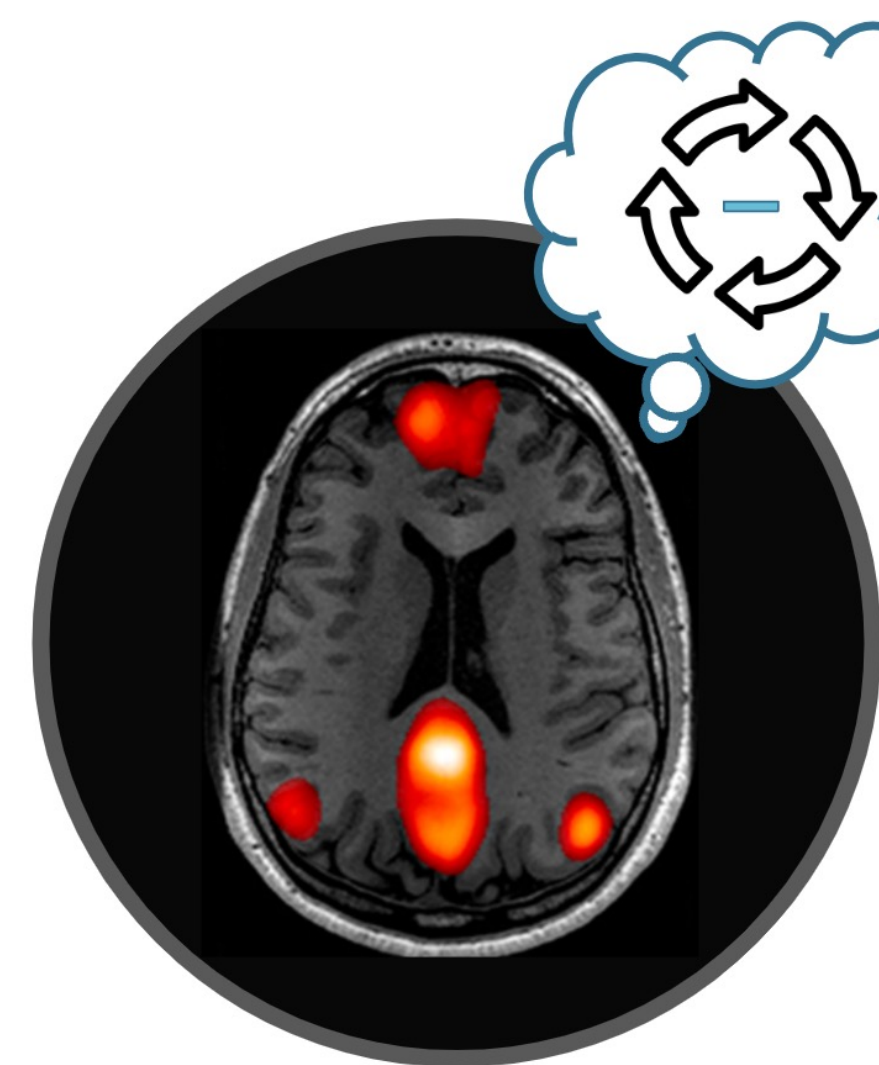
Methods: Twenty individuals with diagnosed depression were enrolled in this open-label case series. They completed up to eleven ultrasound sessions within a three-week period. They also completed symptom self-report surveys and interviews before, during, and after treatment.

Hypotheses: It was hypothesized that transcranial-focused ultrasound targeting a major hub of the default mode network, the anterior medial prefrontal cortex, will improve depression symptoms and repetitive negative thought.

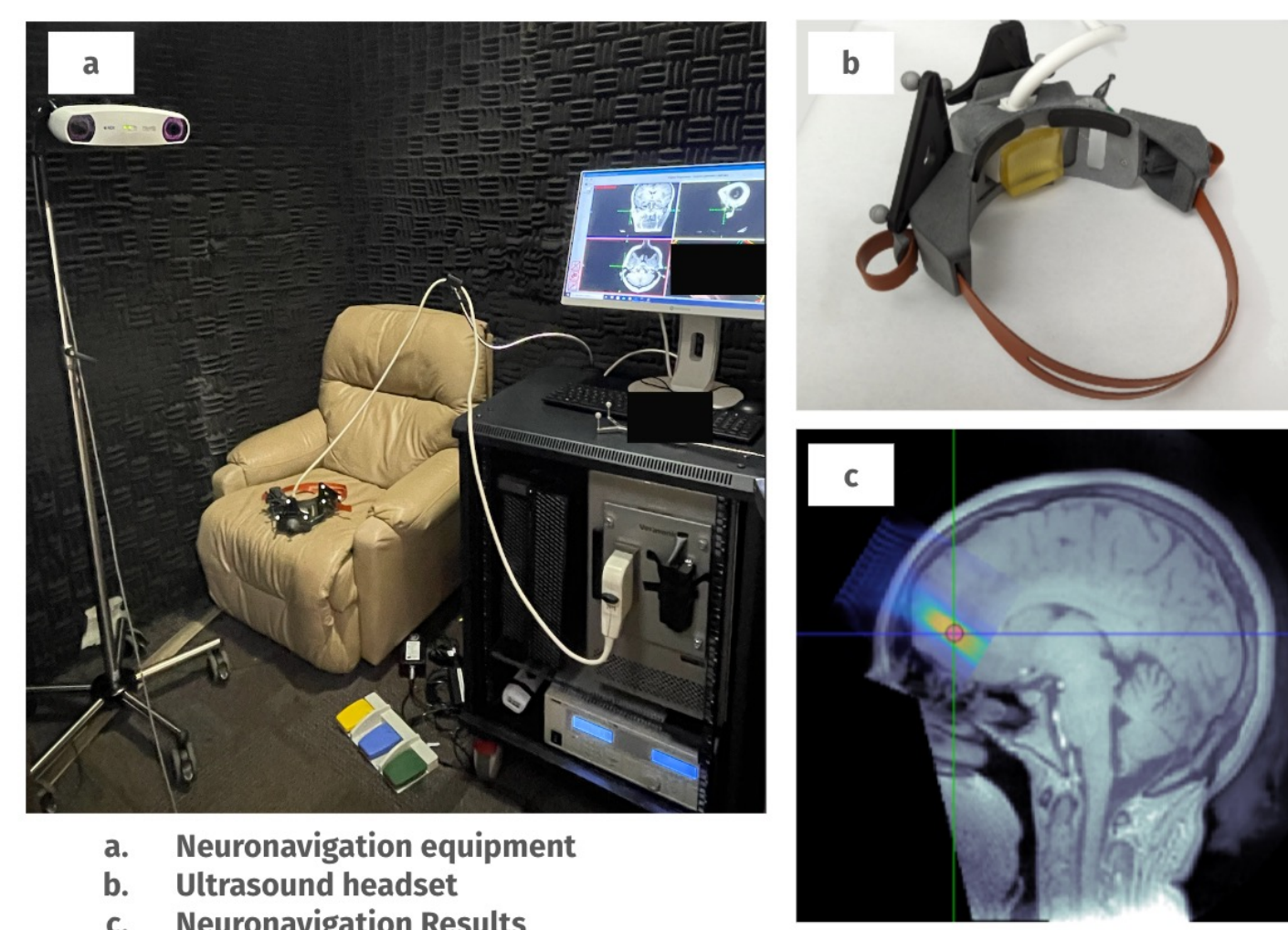
Results: There was a significant reduction in depression symptoms and repetitive negative thought after a three-week transcranial focused ultrasound treatment protocol. Two participants dropped before treatment completion.

Conclusion: These findings suggest that transcranial focused ultrasound holds promise as a treatment for depression.

Background



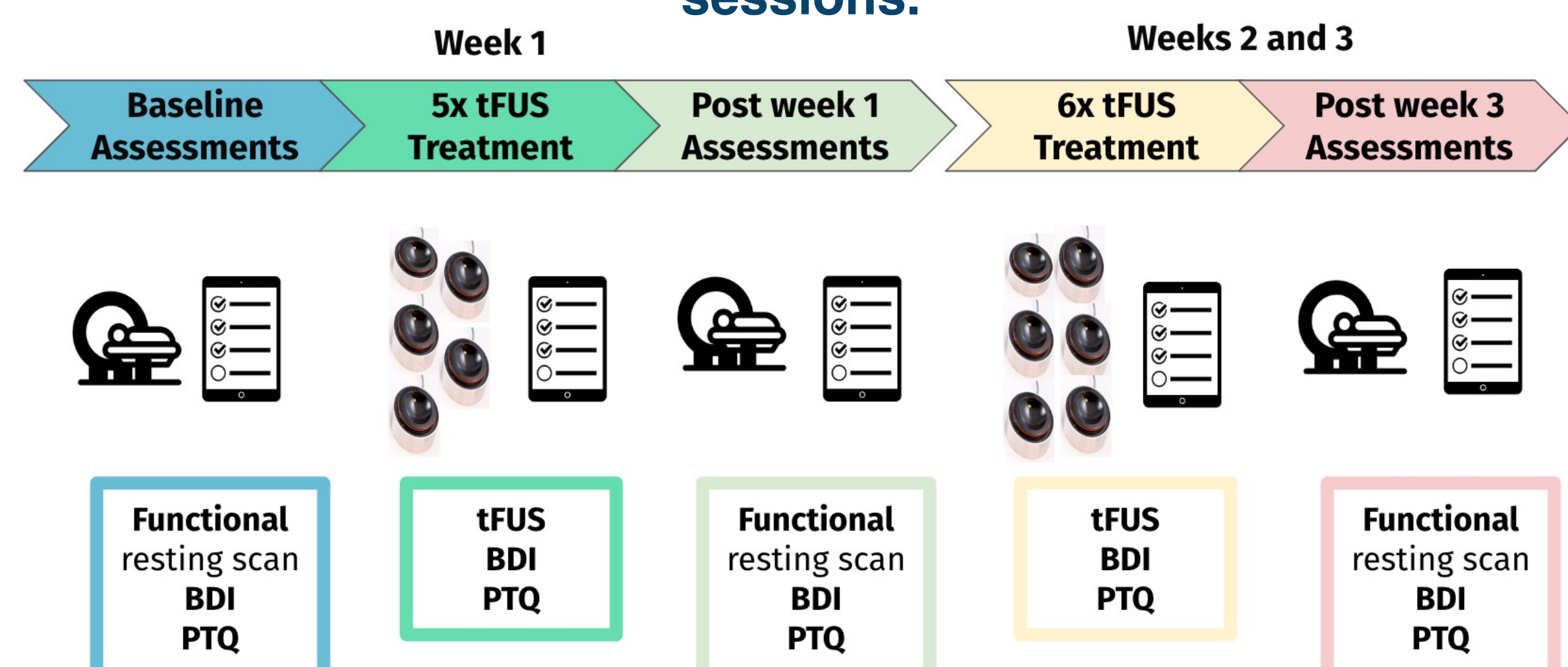
Repetitive Negative Thought (RNT) has been identified as a potential maintaining factor in depression, such that those who exhibit higher degrees of RNT endorse greater depression symptoms (Taylor & Snyder, 2021). **The Default Mode Network (DMN)** plays an important role in depression wherein it has been linked to RNT (Sheline et al., 2010). In depressed individuals, this network appears to be hyper-connected, which, in turn, is thought to promote RNT (Shi et al., 2015).



Non-invasive Transcranial Focused Ultrasound Stimulation (tFUS) is a promising tool for the treatment of depression (Resnik et al., 2020; Sanguinetti et al., 2020). tFUS directs a low-intensity (nonthermal) focused ultrasound beam that passes safely through the skull (Fini & Tyler., 2017).

Methods

Twenty participants with diagnosed depression completed a series of MRI scans, surveys and interviews, and up to 11 tFUS sessions.



Beck Depression Inventory-II (BDI)
Perseverative Thinking Questionnaire (PTQ)

Results

Participant Demographics

Demographics	N = 20
Age (M/SD)	30.35 (10.04)
Gender (F/M/Other; %)	75 / 20 / 5
Years of education (M/SD)	13.83 (1.93)
Race (%)	
White	45
Black	10
Chinese	5
Middle Eastern	5
Indian	5
Unknown	30
Ethnicity (%)	
Hispanic	0
Non-Hispanic	70
Unknown	30
Employment (%)	
Full-time	15
Student	15
Part-time	45
Unemployed	25
Baseline BDI-II (M/SD)	38.85 (9.34)
Baseline PTQ (M/SD)	44.35 (6.24)
Baseline HDRS (M/SD)	19.90 (6.34)
Depression onset (Early/Teen/Adult) (%)	55/ 25 / 20

Table 1. Participant demographics. In addition to the information provided on the table, 50% of participants had a comorbid diagnosis (e.g., 85% of participants had comorbid anxiety & stress-related disorders) and 50% of participants were currently on psychiatric medication.

Results

Response and remission after tFUS treatment

	Responded (50% reduction)	Remitted (HDRS <8; BDI<13)
Beck Depression Inventory (BDI-II)	60%	35%
Hamilton Depression Rating Scale (HDRS)	45%	35%

Results

There was a significant reduction in self-report and interview depression symptoms after tFUS treatment

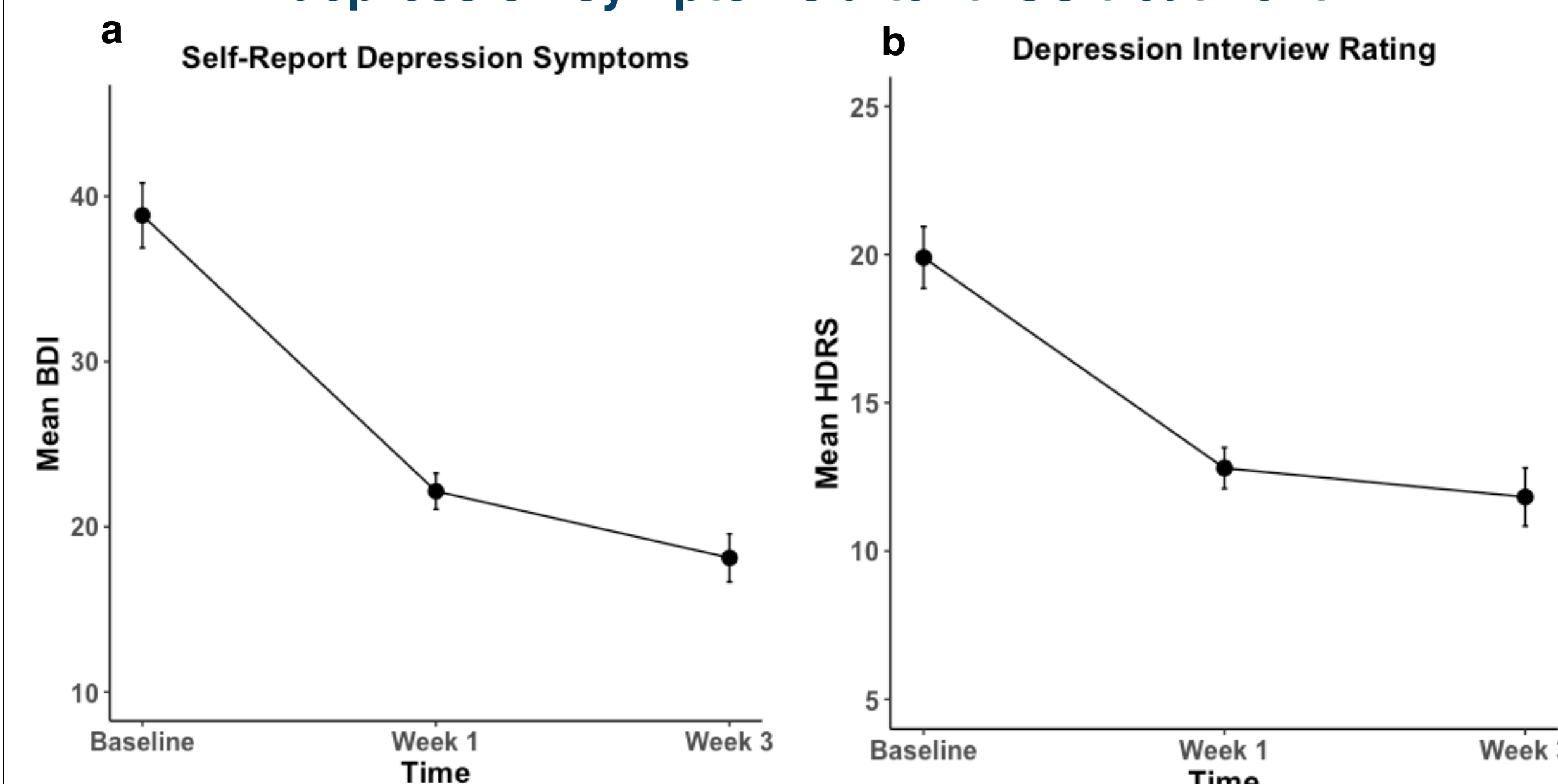


Figure 1. a) Multi-level model assessing change in BDI-II over the course of ultrasound treatment. There was a significant reduction in depression symptoms after ultrasound treatment. **b)** Multi-level model assessing change in HDRS over the course of tFUS treatment. There was a significant reduction in depression symptoms after tFUS treatment. Error bars are within-subject.

Results

There was a significant reduction in repetitive negative thought after tFUS treatment

Self-Report Repetitive Negative Thinking

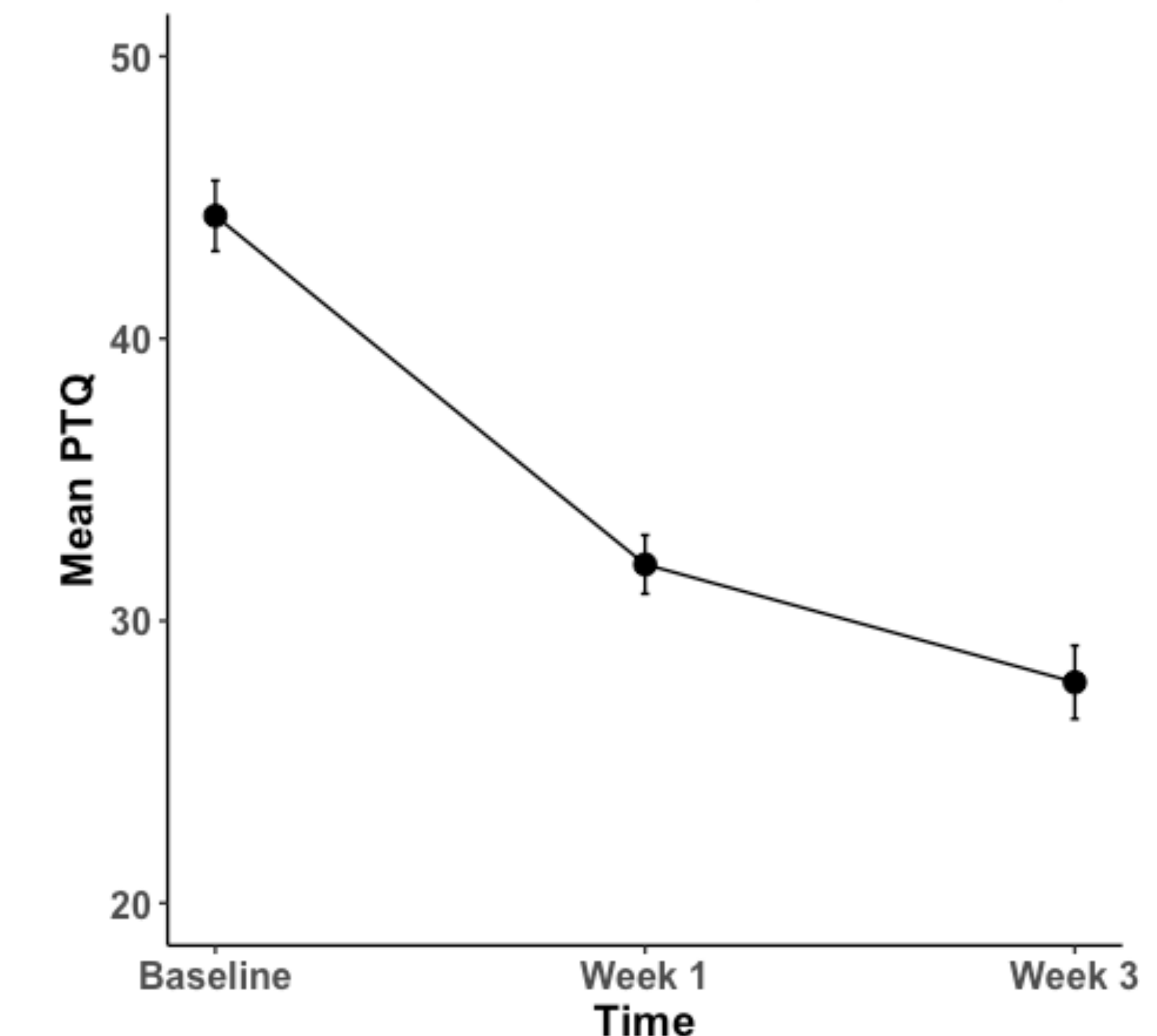


Figure 2. Multi-level model assessing change in RNT over the course of ultrasound treatment. There was a significant, reduction in RNT after tFUS treatment. Error bars are within-subject

Results

Those with greater change in depression symptoms experienced a greater change in repetitive negative thought.

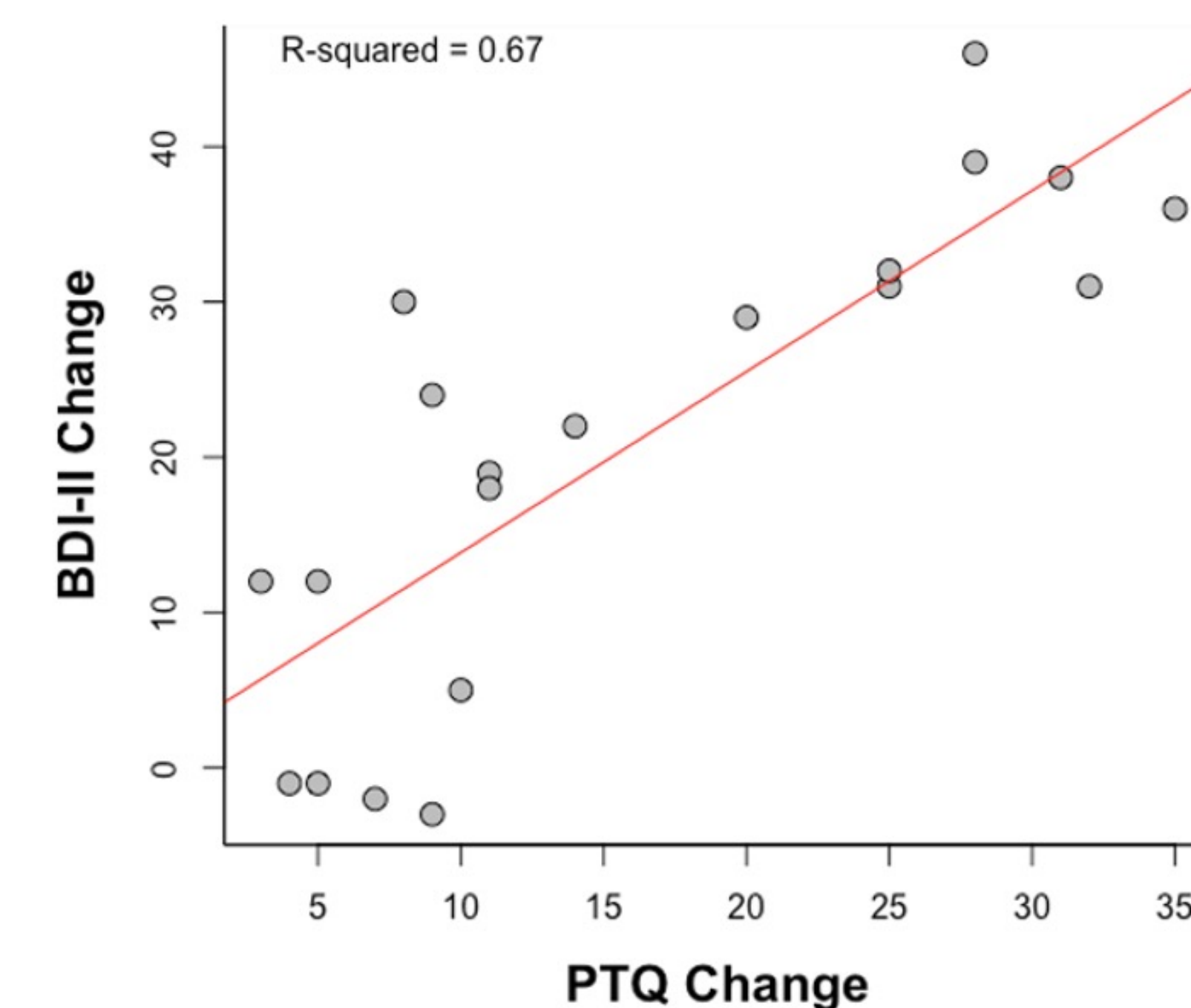


Figure 3. Linear regression between depression symptom change and RNT change. There was a significant, positive relationship between change in depression symptoms and change in RNT.

Conclusion & Next Steps

Significant decreases in depression occurred on the self-report, 11.3 ($p > 0.001$, $CI = -14.68, -8.15$) and interview depression ratings, 4.3 ($p > 0.001$, $CI = -6.21, -2.43$), respectively, after tFUS treatment. Additionally, RNT significantly decreased by 8.53 ($p > 0.001$, $CI = -11.01, -5.79$), and there was a significant relationship between change in depression and change in RNT ($R^2 = 0.67$, $F = 36.84$ (1, 18), $p < 0.001$). These findings suggest that tFUS holds promise as a treatment for depression. Next steps include exploring changes in DMN connectivity and exploring the relationship between change in depression symptoms and change in DMN connectivity after treatment. A RCT with a larger sample and sham control group is required to confirm findings.

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