A Major Multicenter Longitudinal Study of Tinnitus Rehabilitation for War Veterans

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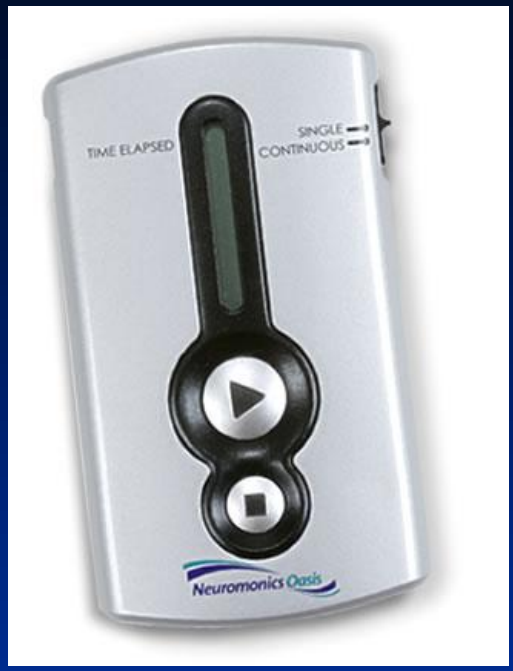
Neuromonics
Tinnitus Treatment

University of Colorado Boulder

Background

- Tinnitus is one of the most frequent disorders suffered by war veterans, and many clinicians are unsatisfied by usual treatment options
- Neuromonics Tinnitus Treatment has been used by more than 1,000 war veterans and active duty soldiers in the USA
- Neuromonics has been the subject of several independent studies on these American Veterans (e.g. White, 2009; Benton, 2010)
- Two more military studies are underway in USA
- So far, Neuromonics has only been available for Australian war veterans on a case-by-case basis

Neuromonics Tinnitus Treatment



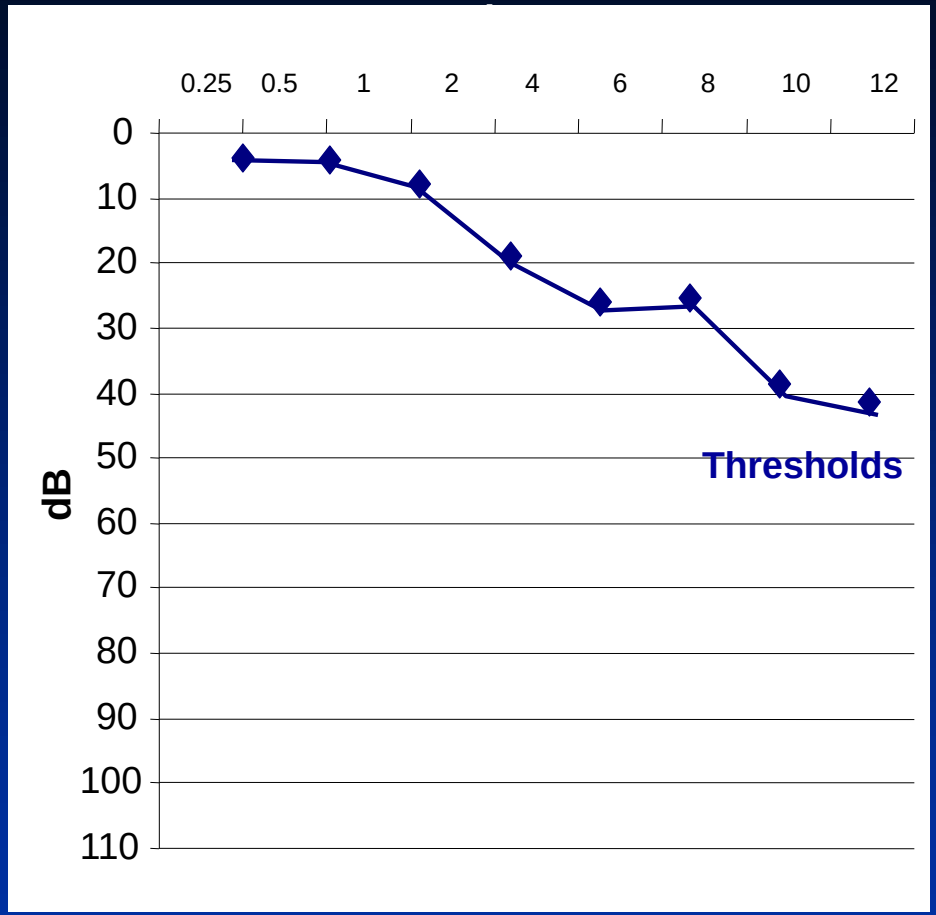
1. Novel (patented) acoustic therapy
   Individually programmed (with compensation for hearing loss)
   Delivered via a purpose-built FDA-cleared medical device

2. 

6 month program of support, monitoring, collaborative counseling and education from a specialist clinician

Customisation: Spectral Modification

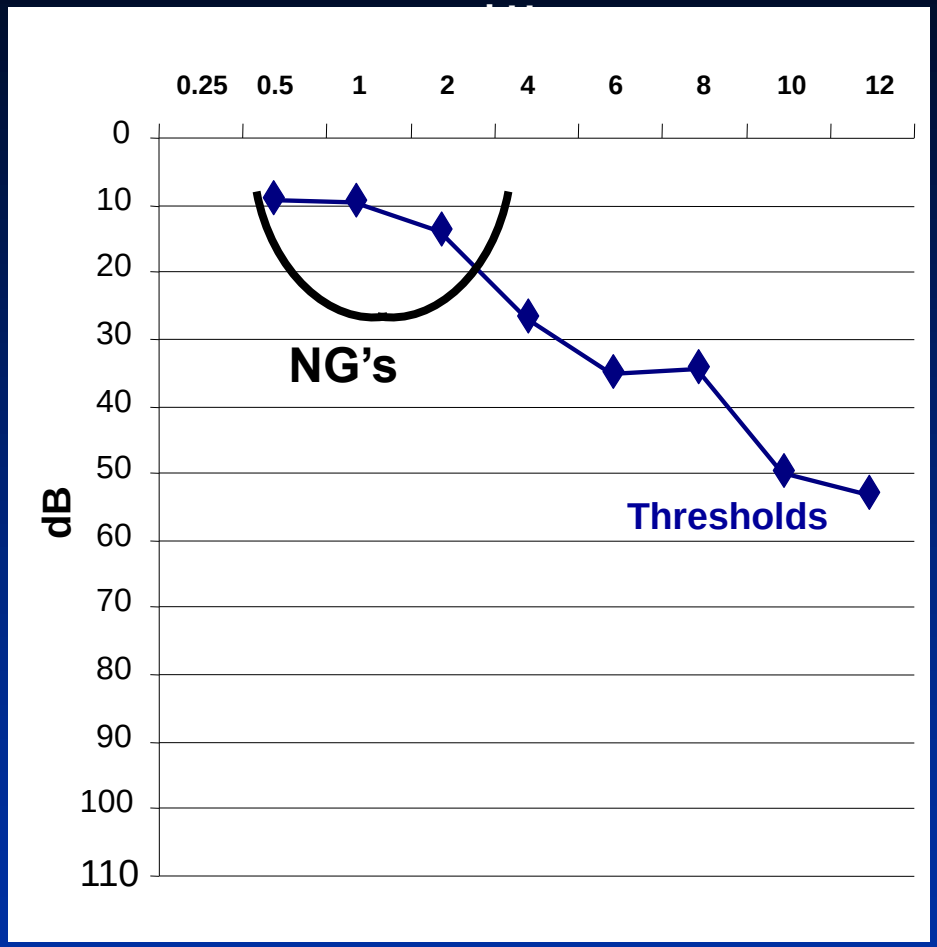
- Typical tinnitus sufferer has hearing loss >4kHz



Mean Hearing Thresholds of Typical Clinic Patient Sample

Customisation: Spectral Modification

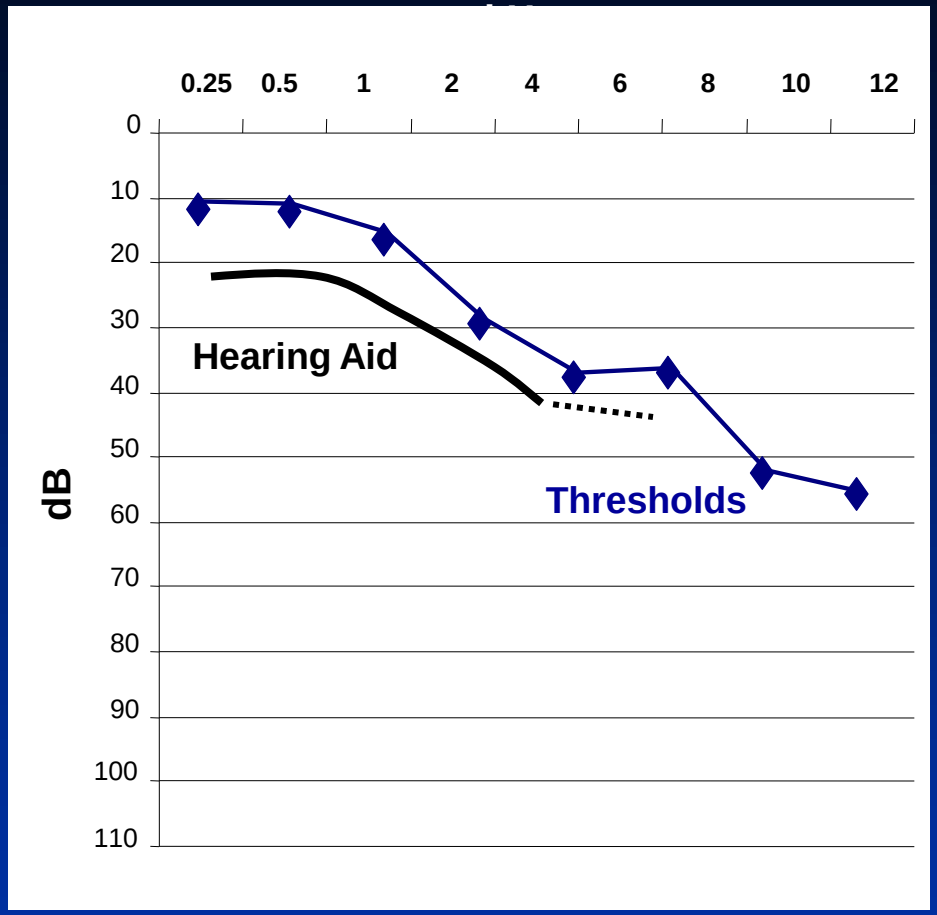
- Maskers/ noise generators provide little stimulus above 4kHz…
- …unless uncomfortably loud in speech range
- …particularly for those with decreased sound tolerance



Spectral Composition of NG's vs. Hearing Thresholds of Typical Clinic Patient Sample

Customisation: Spectral Modification

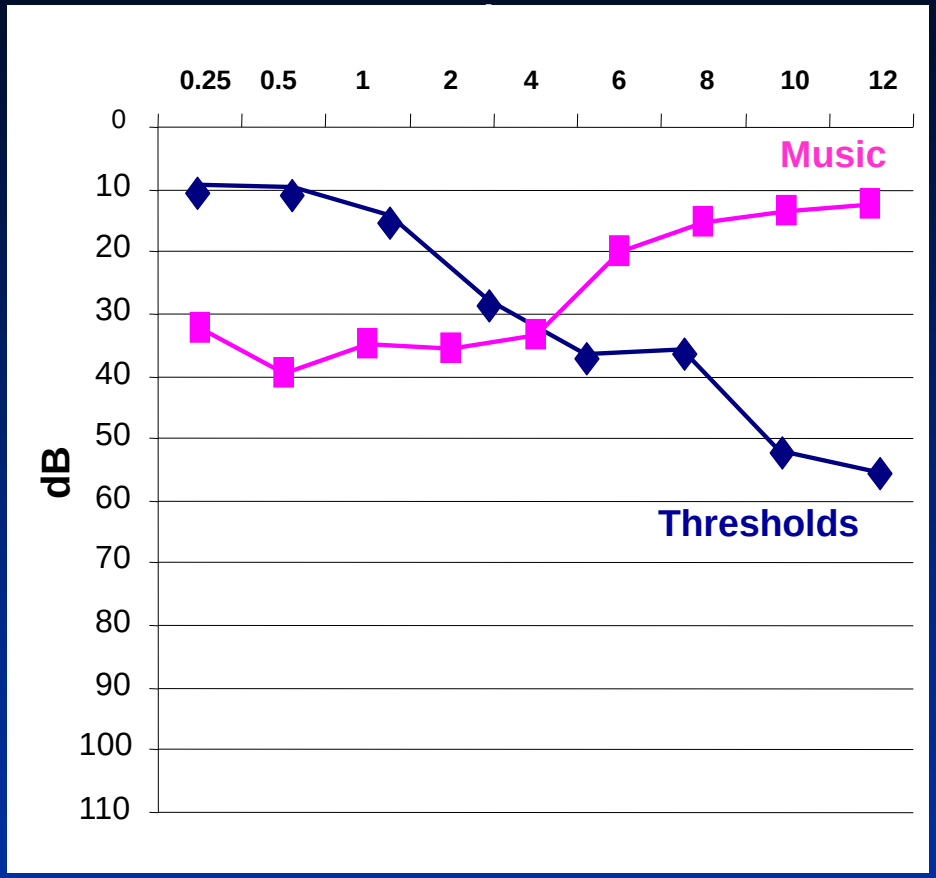
- Hearing aids also
  - limited in actual frequency range
  - problematic with fluctuating inputs
  - Problematic with decreased sound tolerance
  - Not often useful at peak distress times of sleep, relaxation & concentration



Spectral Composition of H/A's vs. Hearing Thresholds of Typical Clinic Patient Sample

Customisation: Spectral Modification

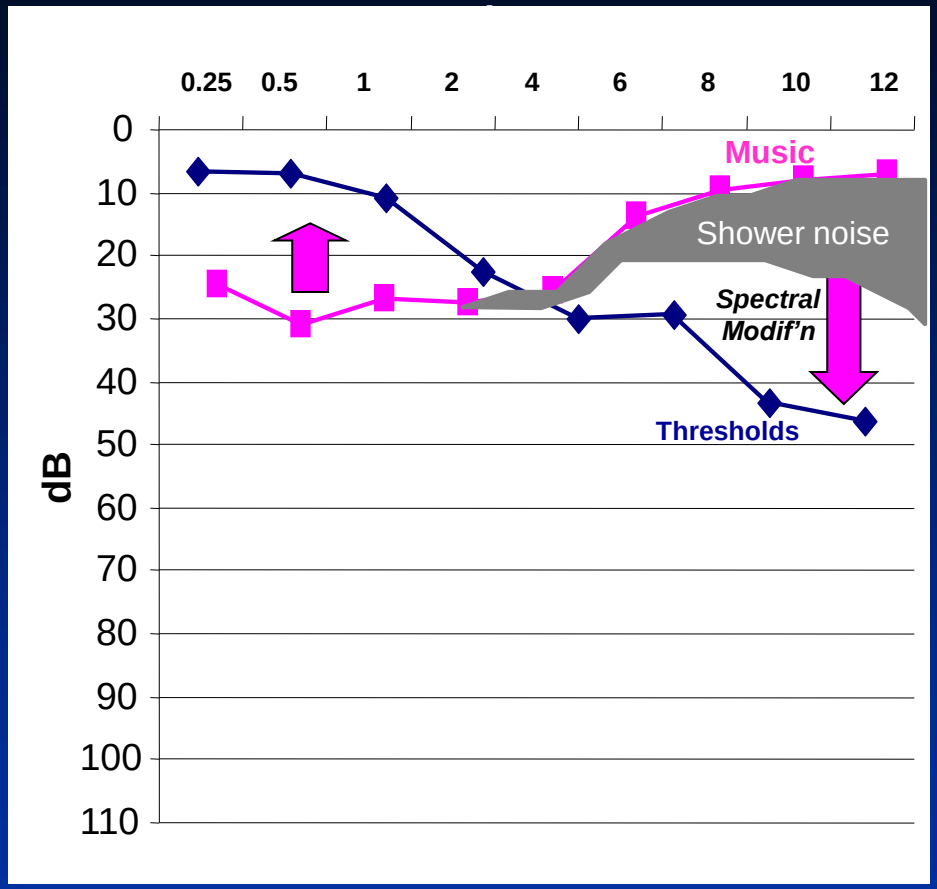
- Normal music has low frequency bias
- (Even this long-term spectral average of this source music used as a basis for neuromonics)
- This is the inverse of what is needed for true broad band stimulation of all neural pathways effected by auditory deprivation



Spectral Composition of Music vs. Hearing Thresholds of Typical Clinic Patient Sample

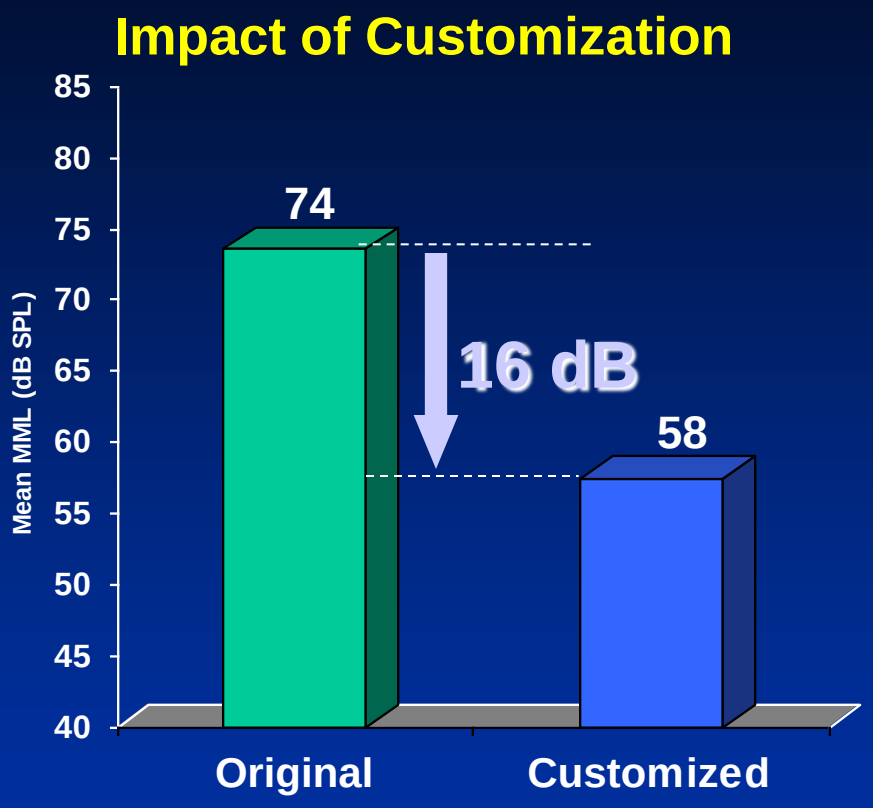
Customisation: Spectral Modification

- NTT's customization algorithms for each patient's blend of music & noise ensures:
  - max stimulation of all auditory pathways
  - compensation for asymmetry
  - control of inter-aural phase relationships
  - Minimizes listening volume required to get high levels of relief



Spectral Composition of Music vs. Hearing Thresholds of Typical Clinic Patient Sample

Individualized Spectral Modification



Trial 3, 2 Stage group, n=19

- Enables interaction with tinnitus perception:
  - at comfortable volume
  - despite hearing loss & decreased sound tolerance
- Speech intelligibility barely effected
- Directly facilitates sleep onset, relaxation, & concentration

Davis, P.B., Paki, B., & Hanley, P.J. (2007). The Neuromonics Tinnitus Treatment: Third Clinical Trial. *Ear & Hearing*, 28: 242-259.

Clinical Studies

#	Study	n	Description	Location	Success
1	T1 – Feasibility	30	Neuromonics, Single Arm	AUS	N/A
2	T2 – NTT vs. SOC (2008)*	50	Neuromonics, TRT vs. counseling alone (RCT)	AUS	86%
3	T3 – 1 vs. 2 Phase (2007)*	35	Neuromonics, Dose Study (RCT)	AUS	90%
4	Private Practice (2008)*	470	Neuromonics, Multiple Tiers of patients	AUS	92%†
5	Lions Ear Institute (2008)*	29	Independent, Single Arm	AUS	75%††
6	Oregon Tinnitus (2008)*	24	Independent, Single Arm	US	72%
7	Tavora TRI (2009)*	25	Independent, Single Arm, non-std pts	AUS	90%
8	Tavora AAA (2010)*	70	Independent, Single Arm, registry	US/AUS	75%
9	CALM (2011)*	51	Independent, Single Arm	US	81%††
10	Hollywood VA (2009)*	35	Independent, Single Arm	US / VA	96%††
12	DoD Study1 (Ft. Rucker)	18	Independent, NTT vs. bioFeedback	US / DoD	?
11	AUS Veterans	57	Independent, Single Arm	AUS /DVA	74%
13	DoD Study2 (Ft. Rucker)	40	Independent, NTT vs. noise	US / DoD	?
14	DoD Study3 (Ft. Rucker)	140	Independent, NTT vs. iPod/ TRT counseling	US / DoD	N/A
	TOTAL	1074		AVG	84%

* Paper / poster

† Std/Tier 1 pts with TRQ ≥40% Improved at completion

†† Interim data

Purpose / Aim of the Study

- Aim: to determine the short, mid, and long-term clinical efficacy for war veterans' tinnitus
- Australian Department of Veterans Affairs specifically wanted to determine Neuromonics' effectiveness for patients who were indentified as unresponsive to prior treatments
- Independently determine if NTT also had any effect on general psychological status

Method

- Longitudinal & controlled study of 57 war veterans undergoing the Neuromonics Tinnitus Treatment
- A large sample size over five separate clinics in Australia was used so the results could be generalized to other veteran populations
- Eligibility criteria included that P's had previously attempted other treatments w/out success
- The effect of the tinnitus was measured in the clinic at 2, 4, & 6 months, and by post at 12 & 24 months
- Any incomplete data-points were conservatively treated on the 'last value carried forward' basis

Tinnitus Reaction Questionnaire (TRQ)

- One of the most rigorous & well-established measures of the effect of patient's tinnitus
- 26 questions, five response options
- Maximum composite score of 104
- >17 = sig effect on quality of life
- Δ > 30% considered clinically sig
- Very high correlation with THI (Moruf & Davis 2011)
- TRQ / THI Δ over Tx almost identical

DASS42

- Depression Anxiety Stress Scale
- 42-item self report questionnaire
- Measures three negative emotional states of depression, anxiety and tension/stress
- Well-established psychometric properties
- Can be administered by any health professional
- Each DASS form was sent to the DVA in a sealed envelope for independent analysis

http://www2.psy.unsw.edu.au/groups/dass/

Subjects

- All 57 veterans in the study were male
- Mean age was 64.7 yrs (range 42 to 85 yrs)
- Mean time since tinnitus onset 27.3 yrs (range 3 to 63 yrs)
- Prior treatments included;
  - hearing aids (58%)
  - music (49%)
  - white noise generators/maskers (37%)
  - counseling (25%)
  - medication (11%)

Blast Injury Status

- Not as many active service people in Australia compared with USA
- Blast injury was operationally defined as being within the last ten years (defn?)
- ~27 had history of blast injury, but only 18 in the last decade;
  - many had subsequent noise exposure

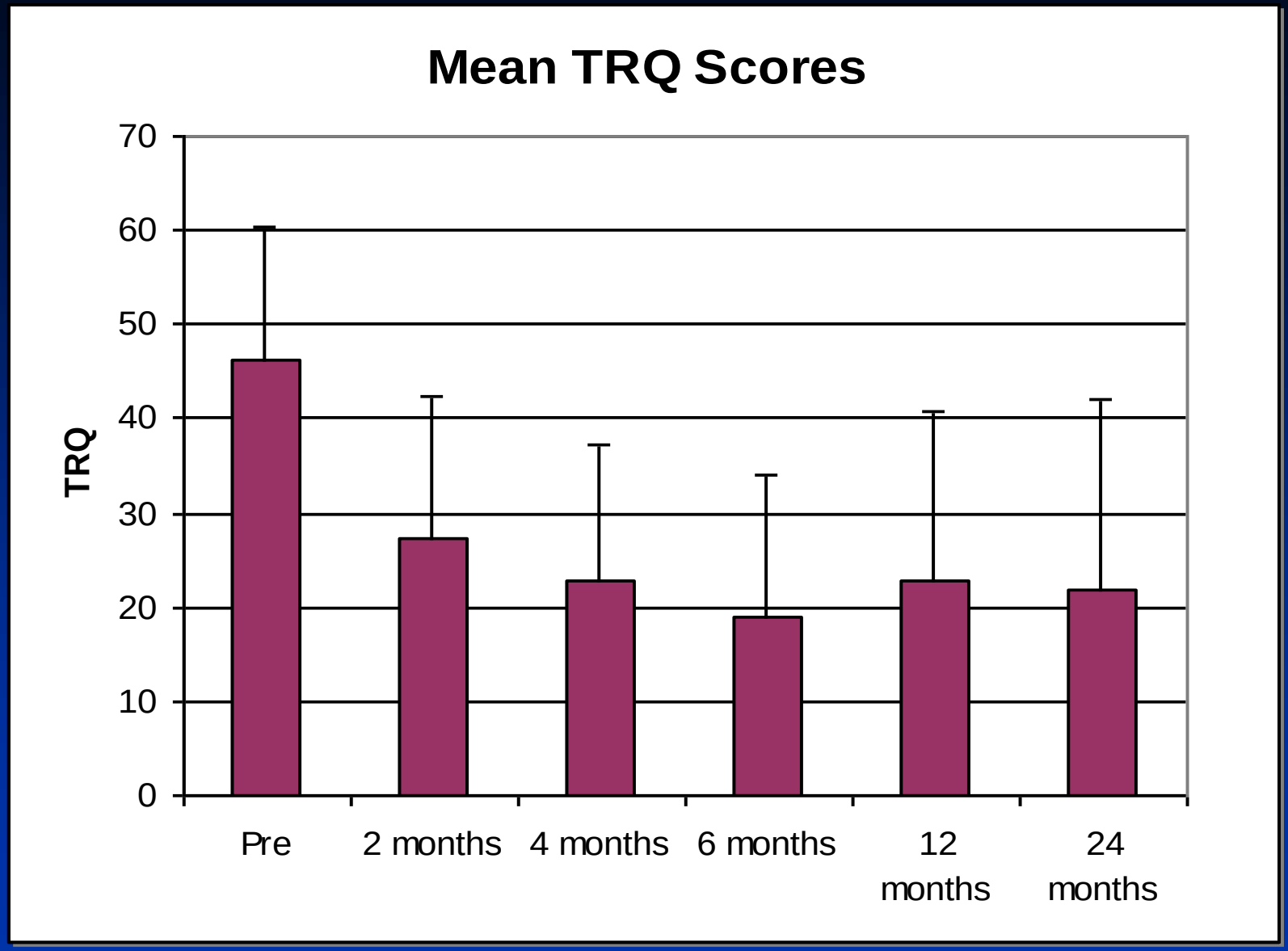
Psych Status

- At Pre-Tx, 26 S's (55.3%) had normal DASS42 scores (all 3 categories)
- 4 identified themselves as having PTSD
- 6 indentified themselves as under extreme stress
- 14 reported undergoing counseling
- 3 reported recent noise making tn worse
- 3 reported cognitive decline
- 8 reported current psychiatric medication (but no change in meds in six months prior to study)

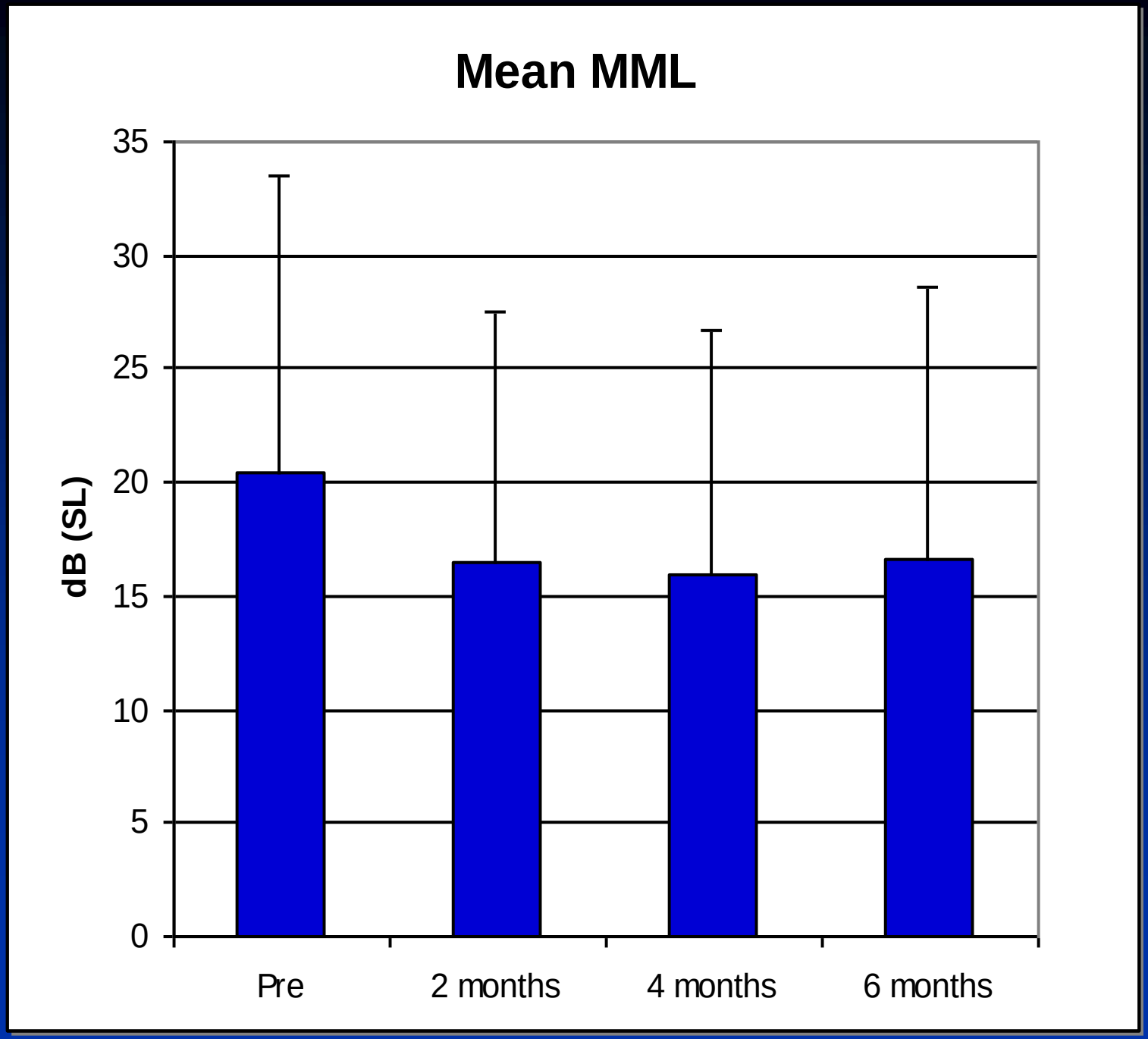
Treatment / Data Status (10/24/11)

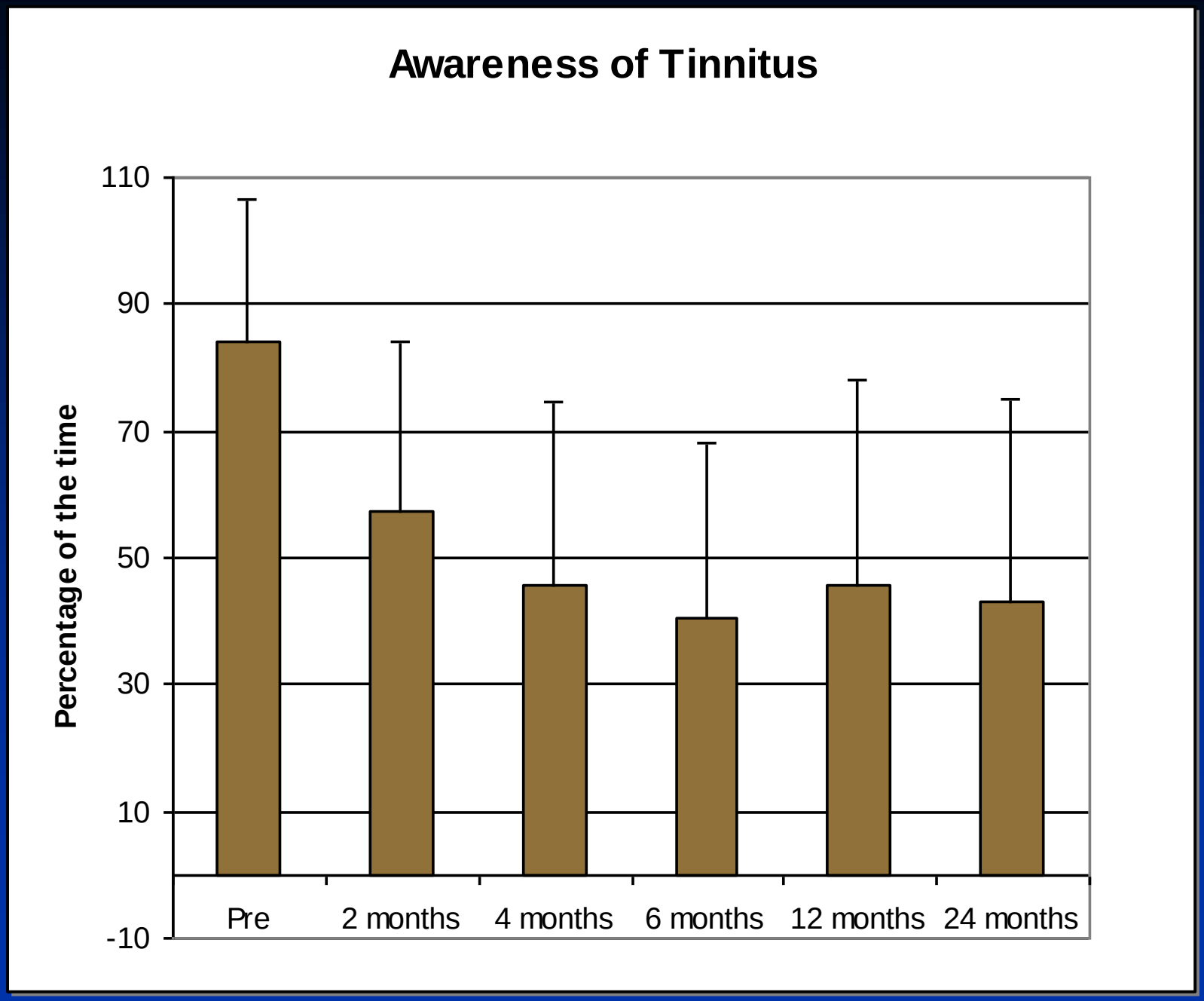
- All 57 veterans completed the formal 6 month treatment period (in some cases up to 9 months)
- All are now self-administering ongoing treatment
- To date, 24 month follow up reviews have been completed for 40 veterans (so this is an interim report)
- A further 9 patients have progressed as far as 12 month reviews, but not yet progressed to 24 months
- One patient withdrew from the study following the 12 month review
- 8 have yet to return 12 month postal assessment forms
- DVA has so far only released Means & SDs of DASS42 data (de-indentified dataset needed for full parametric statistical testing)

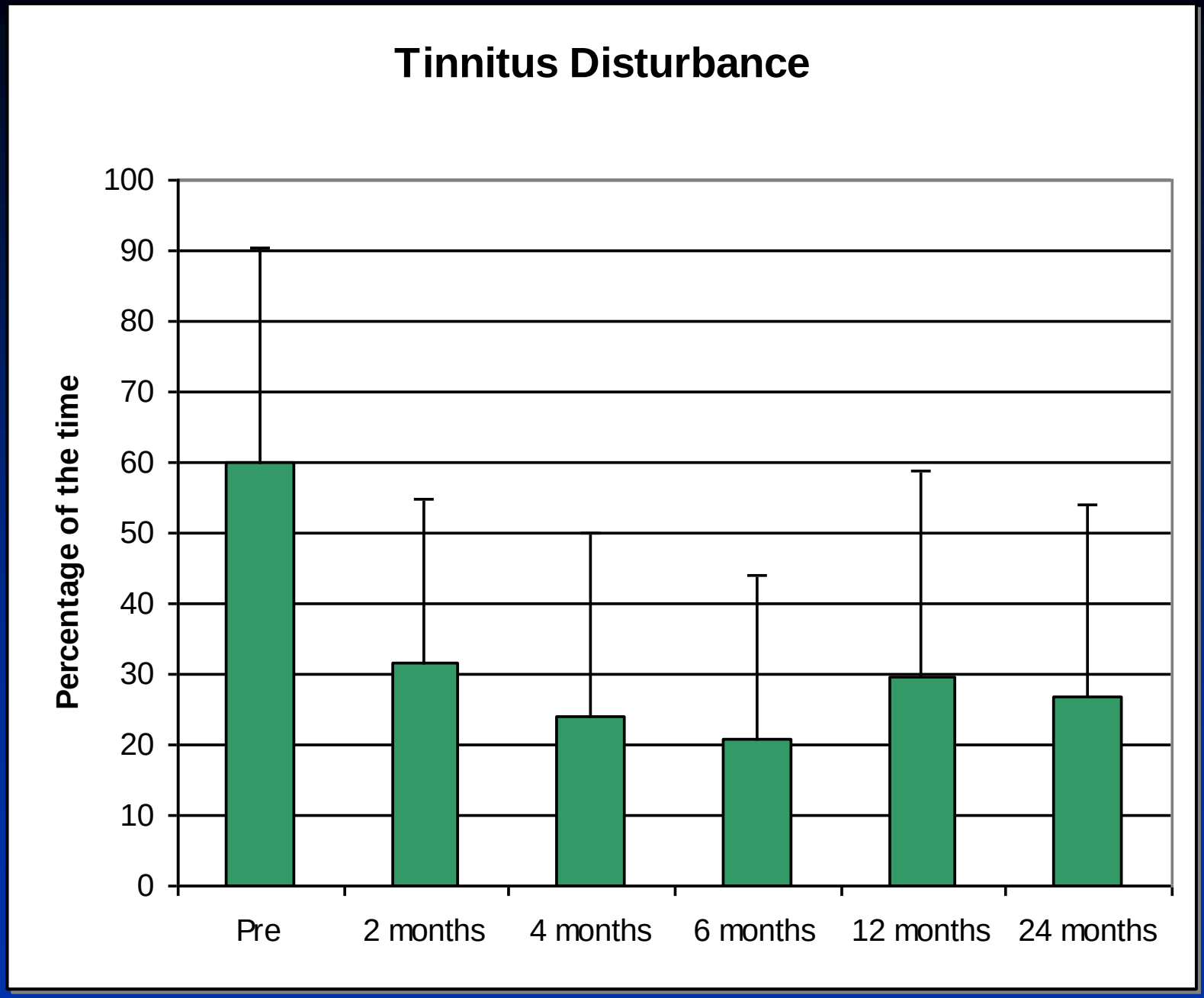
Results



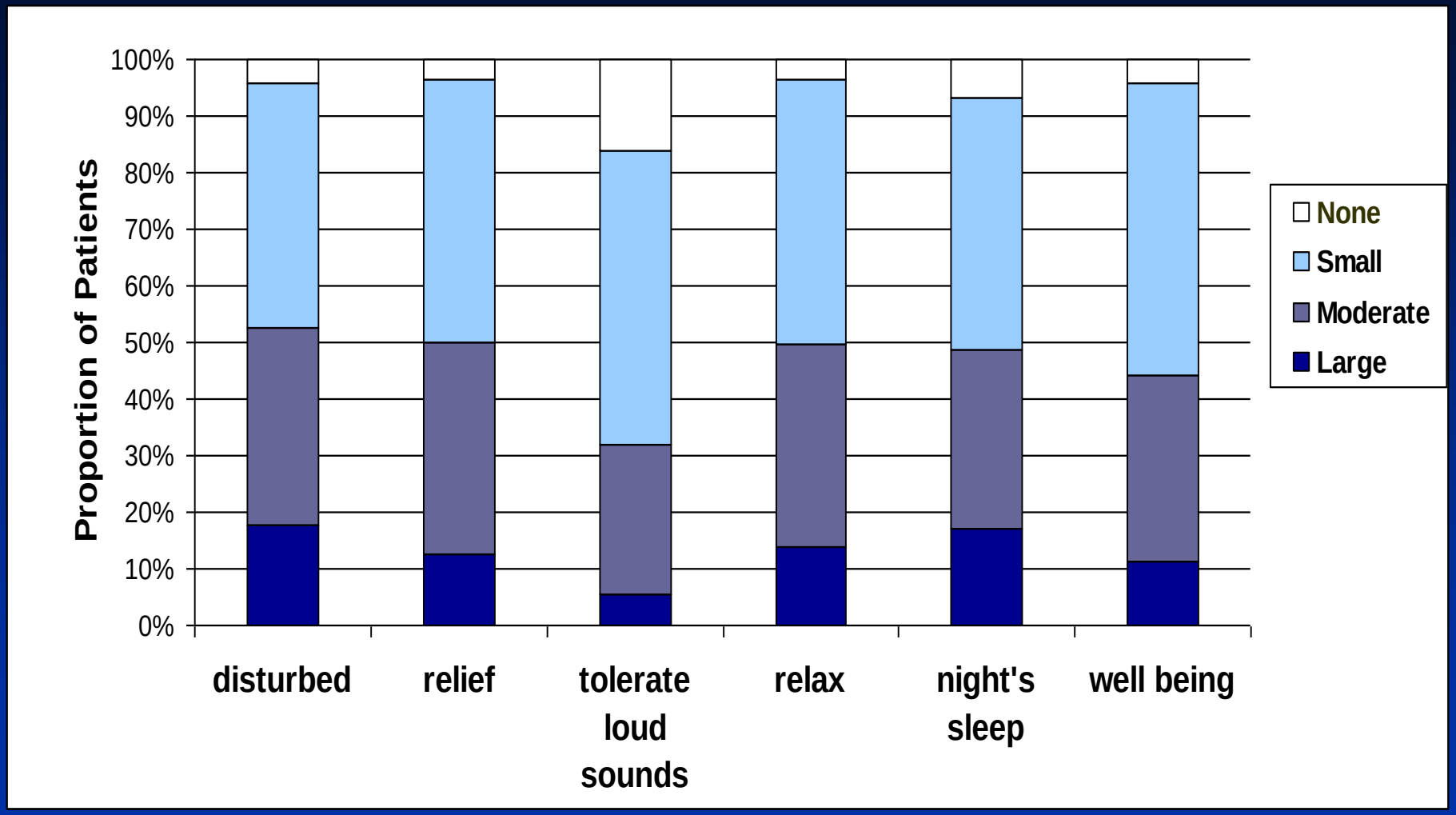
Significant improvements were found at 6 months (t= 11.963, df= 56, p<0.05) and 12 months (t= 9.405, df= 56, p<0.05). NSD from 6mths to 12 & 24mths


Mean MML
dB (SL)
35
30
25
20
15
10
5
0
Pre
2 months
4 months
6 months


Awareness of Tinnitus
Percentage of the time
110
90
70
50
30
10
-10
Pre
2 months
4 months
6 months
12 months
24 months

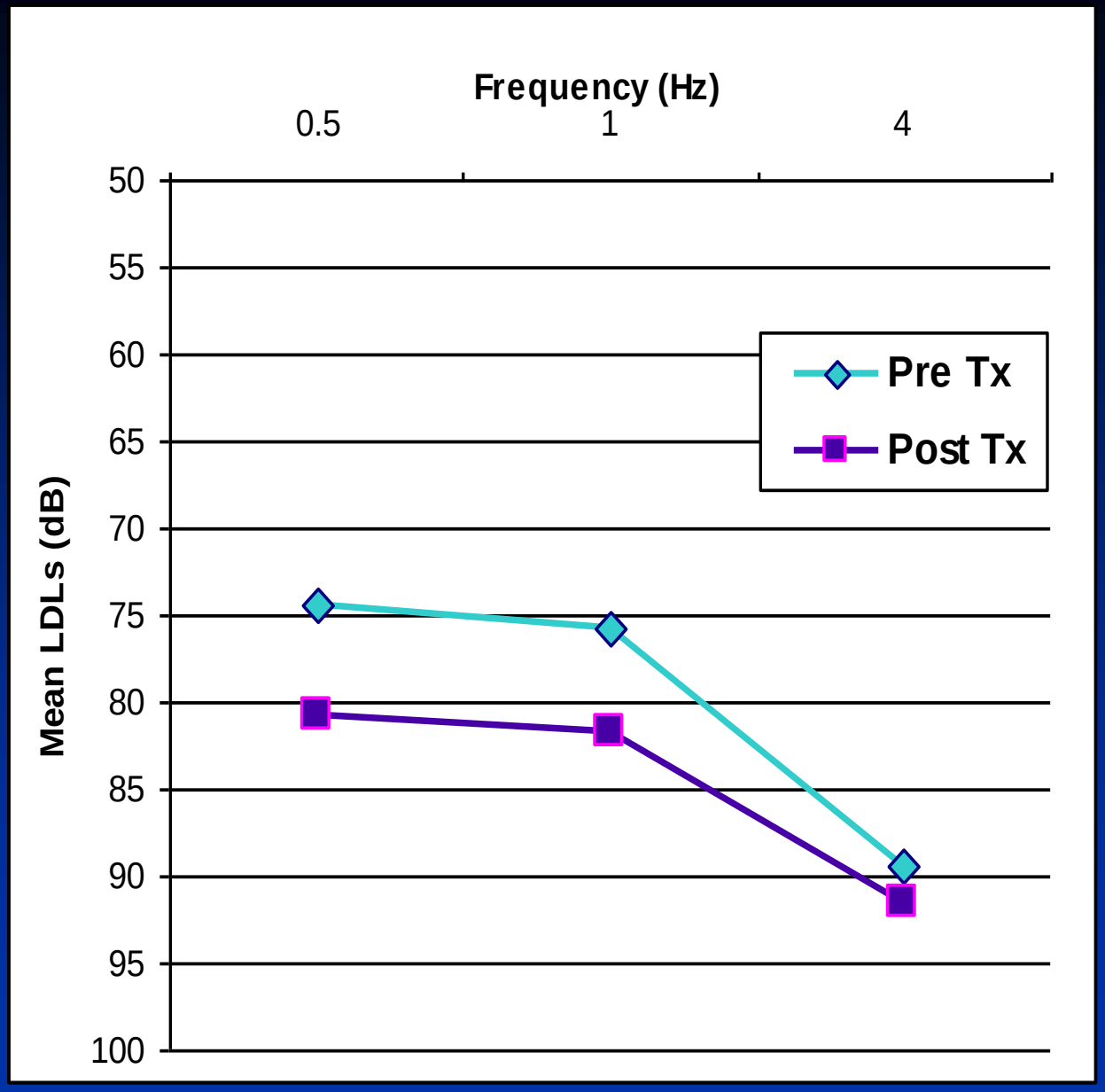

Tinnitus Disturbance
Percentage of the time
100
90
80
70
60
50
40
30
20
10
0
Pre
2 months
4 months
6 months
12 months
24 months

Completion Questionnaires

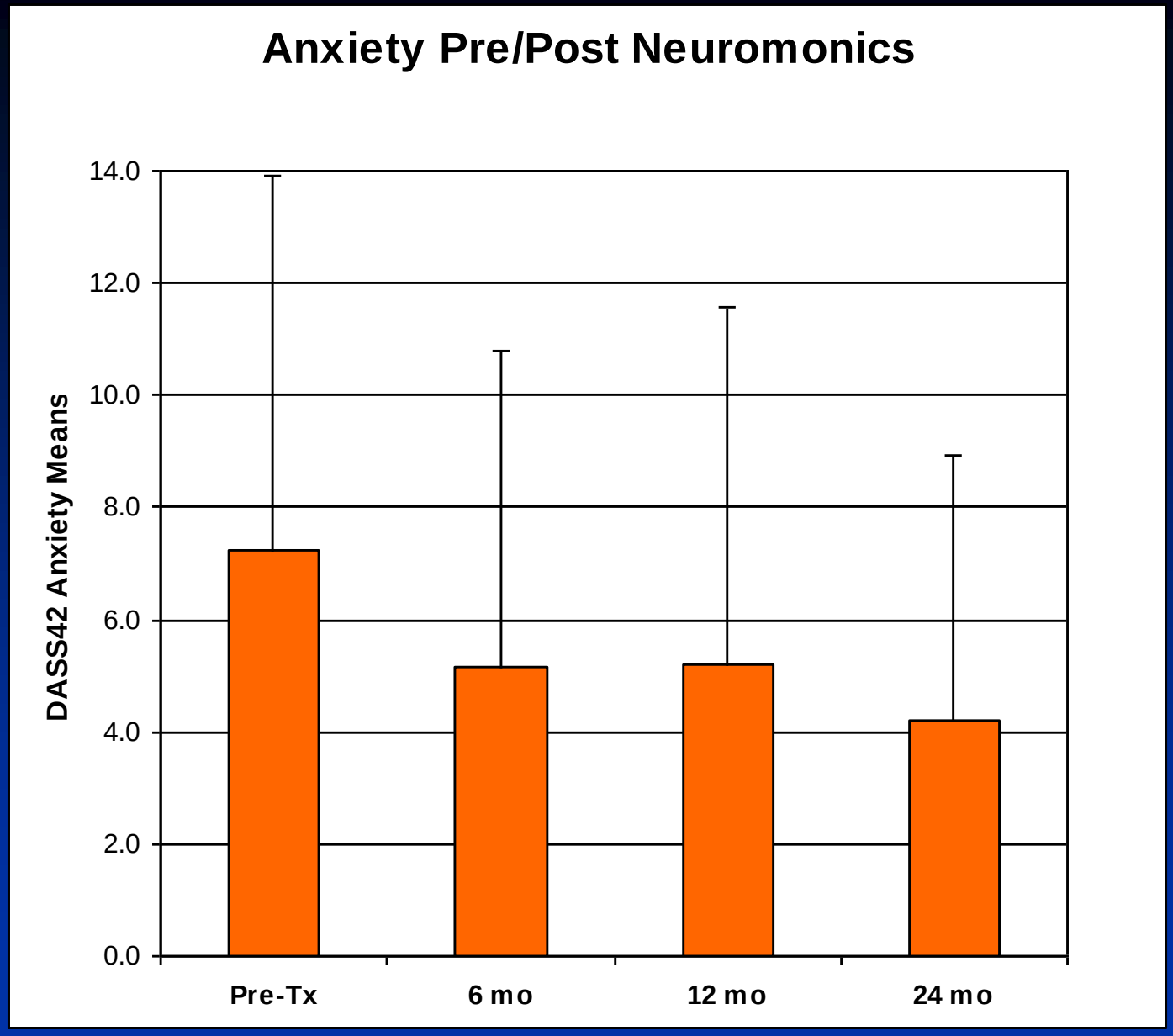


Mean LDL's of all Pt's at Pre-Tx who had decreased sound tolerance (<85 dB 4Freq Av in worst ear)

(Cochlear ceiling effect limits Δ in those who had normal LDL's)

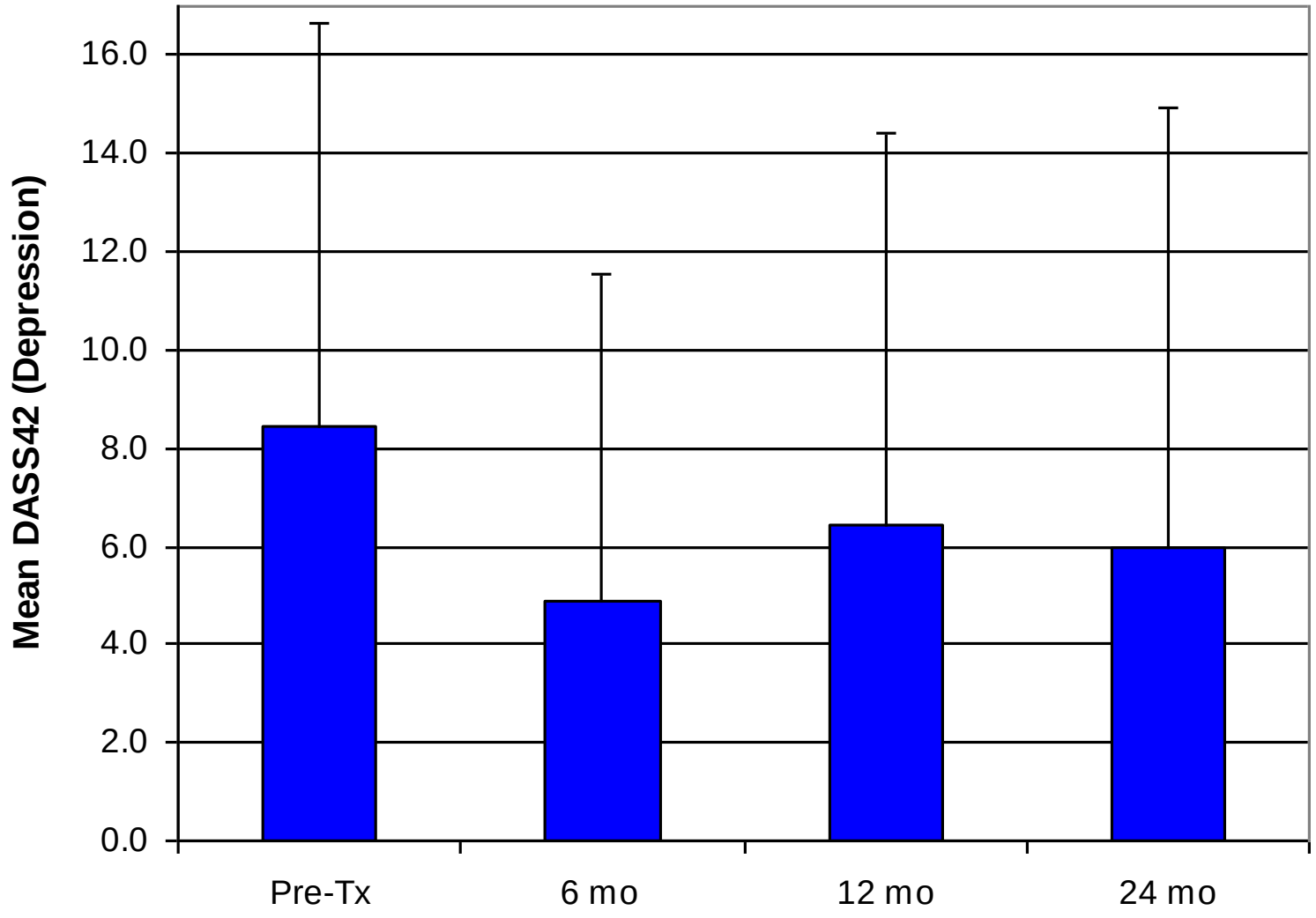


*H/A tolerance improves greatly by Post Tx



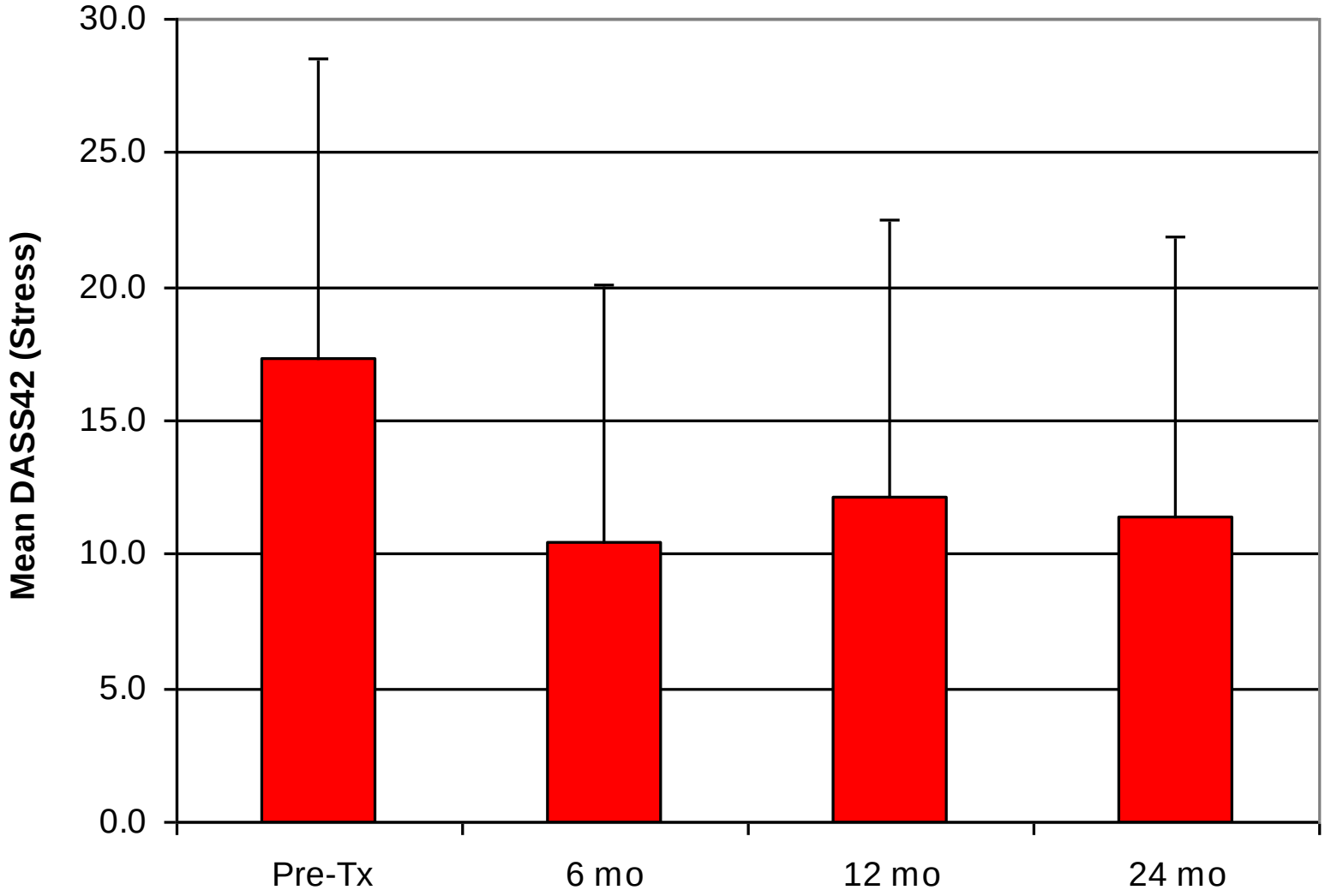
Note: dataset includes more than half the Pts who were normal at Pre-Tx (Ceiling effect)

Depression Pre/Post Neuromonics



Note: dataset includes more than half the Pts who were normal at Pre-Tx (Ceiling effect)

Stress Pre/Post Neuromonics



Note: dataset includes more than half the Pts who were normal at Pre-Tx (Ceiling effect)

Completion Questionnaires

- At the end of the clinical phase of the study, the subjects provided their acceptability ratings;
  - 94% of respondents indicated that they felt the treatment was pleasant to listen to (n=53)
  - 100% of respondents indicated that they felt the treatment was easy to use (n=53)
  - 81% of respondents indicated that they felt the treatment was convenient to incorporate into their daily routine (n=53)
  - 96% of respondents indicated that they would recommend the treatment to others (n=52)

Benefits other than tinnitus (N=30)

“began reading books = enjoyable; didn't do this before”, “I have a tool to control the tinnitus when it is particuarly loud or annoying”, Yes: easier to tolerate tinnitus, can go out more, better able to relax; no longer angry; enjoy life more; better person, much greater tolerance to enclosed areas such as entertainment, particularly group activities, I am more calm about life, I get to sleep better, Yes and no: everything was going OK until my back flared up, I can sit quietly and just relax without the ringing all the time easier to carry out conversation; TV & music not as loud; more relaxed., ability to relax, I will make more attempts at social outings but still stuggle hearing conversation in this type of atmosphere, tinnitus doesn't disturb me as much now”

Other Comments (Cont…)

"more tolerant with family, much calmer; more able to control stressful events., sleeping better being able to back to sleep if awoken during the night, happier now that my tinnitus seems to be more under control, assistance in relaxing, ability to go and stay asleep without use of sleeping tablets or deliberately staying up late a slight improvement only, I am less aware of my tinnitus eg. the noise 60% of the time is less, more sociable and able to accept my tinnitus as an annoyance, being able to better cope with tinnitus, generally not as on edge as before treatment, can hear better, more relaxed and easy going, I can get to sleep and stay asleep"

Effect Size Discussion

- Effect Sizes are ‘building blocks’ of meta-analyses
- A ‘level playing field’ that gives a single measure of how consistently large a treatment really is
- THI & TRQ post Tx change found to be almost identical
- Cohen’s d is a popular effect size calculation technique
- It constitutes the Pre/Post Tx change divided by the variability of it (pooled standard deviation)

$$\overline{ES} = \frac{\overline{X}_{G1} - \overline{X}_{G2}}{s_{pooled}}$$

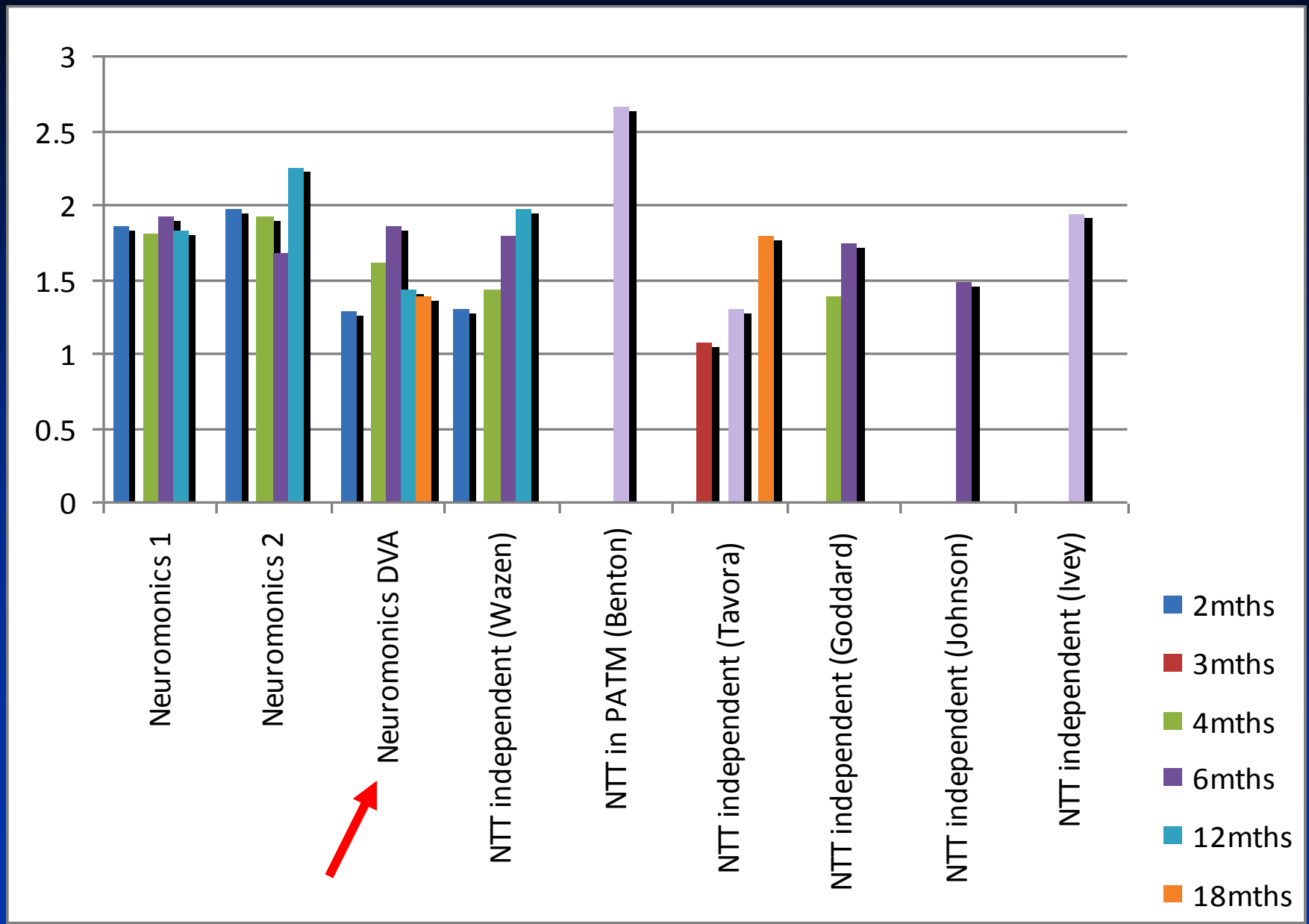
$$s_{pooled} = \sqrt{\frac{s_1^2(n_1 - 1) + s_2^2(n_2 - 1)}{n_1 + n_2 - 2}}$$

Cohen effect sizes are typically interpreted as:

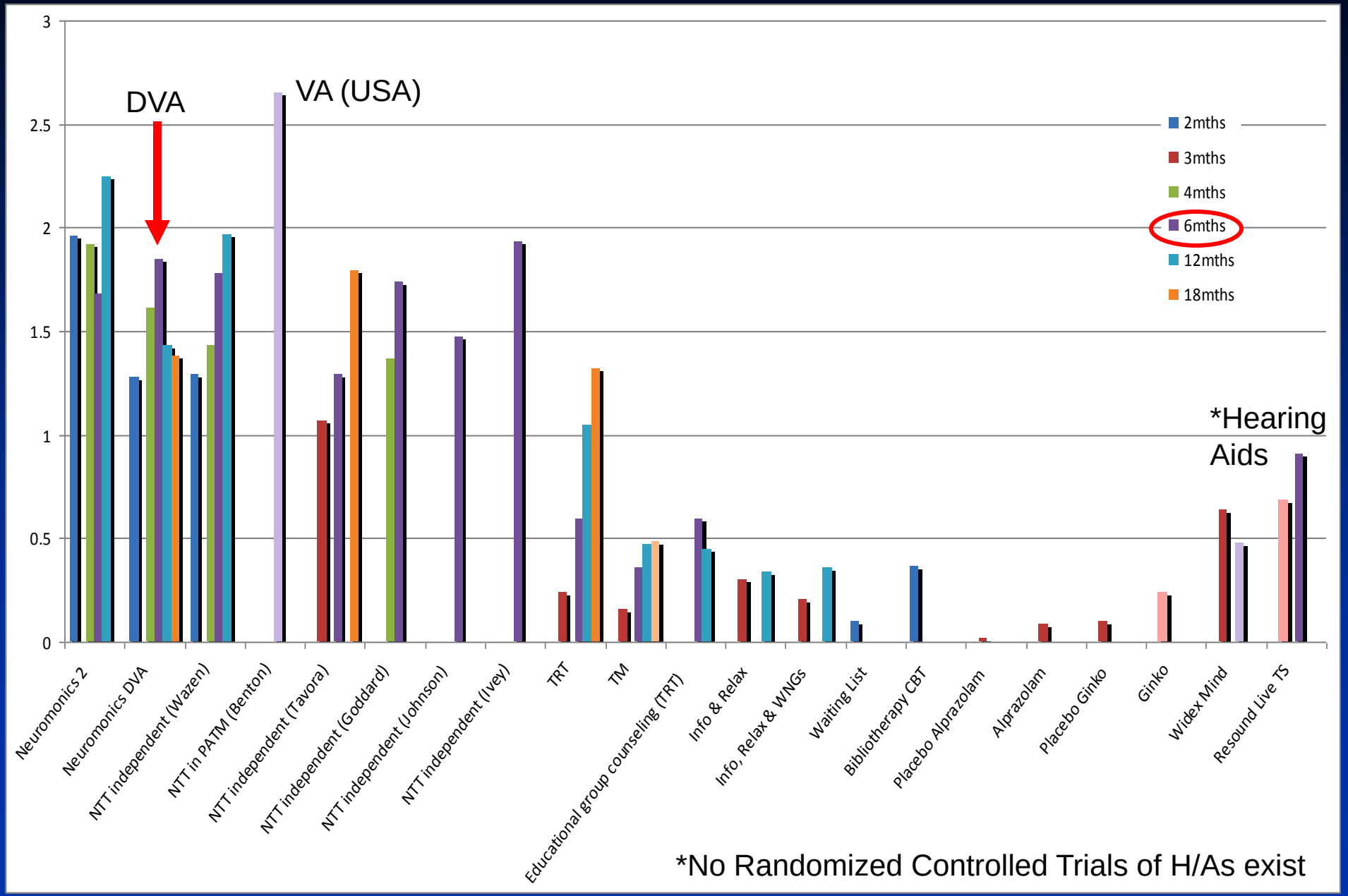
<0.20 = trivial effect
>0.20 and <0.50= minor effect
>0.50 and <0.80 = average effect
>0.80 = substantial effect

Moruf, S., & Davis, P. (2011) Research Poster presented at the American Academy of Audiology, Chicago, April 6-9, 2011

Sponsored Vs Independent Study ES's



Moruf & Davis (2011) Full Effect Size Dataset



Conclusion / What was learned

- Results indicated that the Neuromonics Tinnitus Treatment was efficacious on these war veterans
- Despite this being a cohort who had not responded to prior treatments
- Anxiety, Depression and Stress generally improved (bi-modal distributions, and normal patients can't become 'super normal', so next step should be to separately analyze results just those who had psychopathology at pre-therapy)
- The TRQ effect sizes were found to be in the mid range compared with prior NTT studies
- Gains were typically maintained over the long term

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