

BACKGROUND

- Deficits in working memory (WM) are a common, recalcitrant and functionally disabling symptom of schizophrenia (SCZ) spectrum disorders and have been associated with reduced gamma (35-50Hz) band response (GBR) in frontoparietal regions of the brain.
- EEG-Neurofeedback (NFB) is an operant conditioning methodology used to train individuals to volitionally control brain oscillatory activity.
- NFB has been used to train frontoparietal GBR and improves WM in healthy (HC) populations.
- Therefore, we assessed: 1) whether NFB can be employed to improve GBR in SCZ patients in terms of tolerability and 2) if improved GBR is associated with improvements in WM.
- We hypothesized that increased coherence in gamma oscillations over frontal cortex would correlate positively with increased performance on a working memory task.

METHODS

Subjects

- Three subjects (two male and one female, ages 18- 27), who met DSM-V criteria for SCZ were recruited from University of California, San Diego and Veterans' Administration Healthcare System for an open-label pilot NFB study.
- Subjects remained on their existing medications throughout the study.

Design

- Pre-treatment assessments included EEG (5 minutes eyes closed, 5 minutes eyes open), performance on the n-back (a WM task), and neuropsychological testing using the Matrix Consensus Cognitive Battery (MCCB).
- In a cross-over design, all subjects completed 8 sessions of Gamma-NFB (G-NFB; 2 sessions/week) followed by 8 sessions of active-placebo (AP-NFB) training over frontal cortex (Standard EEG sites, F3 and F4).

Materials & Assessment

- Cognionics 20 channel Dry EEG Cap.
- EEG analysis was conducted in EEGLAB Toolbox via MATLAB; Down sampled: 512Hz - 256 Hz; FIR Filter: 0.5Hz - 120Hz; EEG channel selection was conducted using International 10-20 System; Referenced data to average channels remaining.
- Assigned Cognionics 10-20 Cap20 head model; Artifacts were rejected manually; Conducted independent component analysis (ICA); Rejected noisy components; Final analysis of EEG data reviewed via STUDY function in EEGLAB

Neurofeedback Procedure:

- Subjects seated in front of a computer screen.
- Electrodes record brain waves from frontal cortex on sites (F3, F4) and "feedback" higher gamma synchrony as success on game
- Progressive increase in threshold required to receive positive feedback from game; Subjects choose game or DVD; Set the success threshold 75%
- Same procedure on sham but different frequency (alpha)

RESULTS: Evidence of Brain Training

EEG-NFB training threshold was increased in all subjects over 8 weeks of gamma-NFB, indicating a training effect.

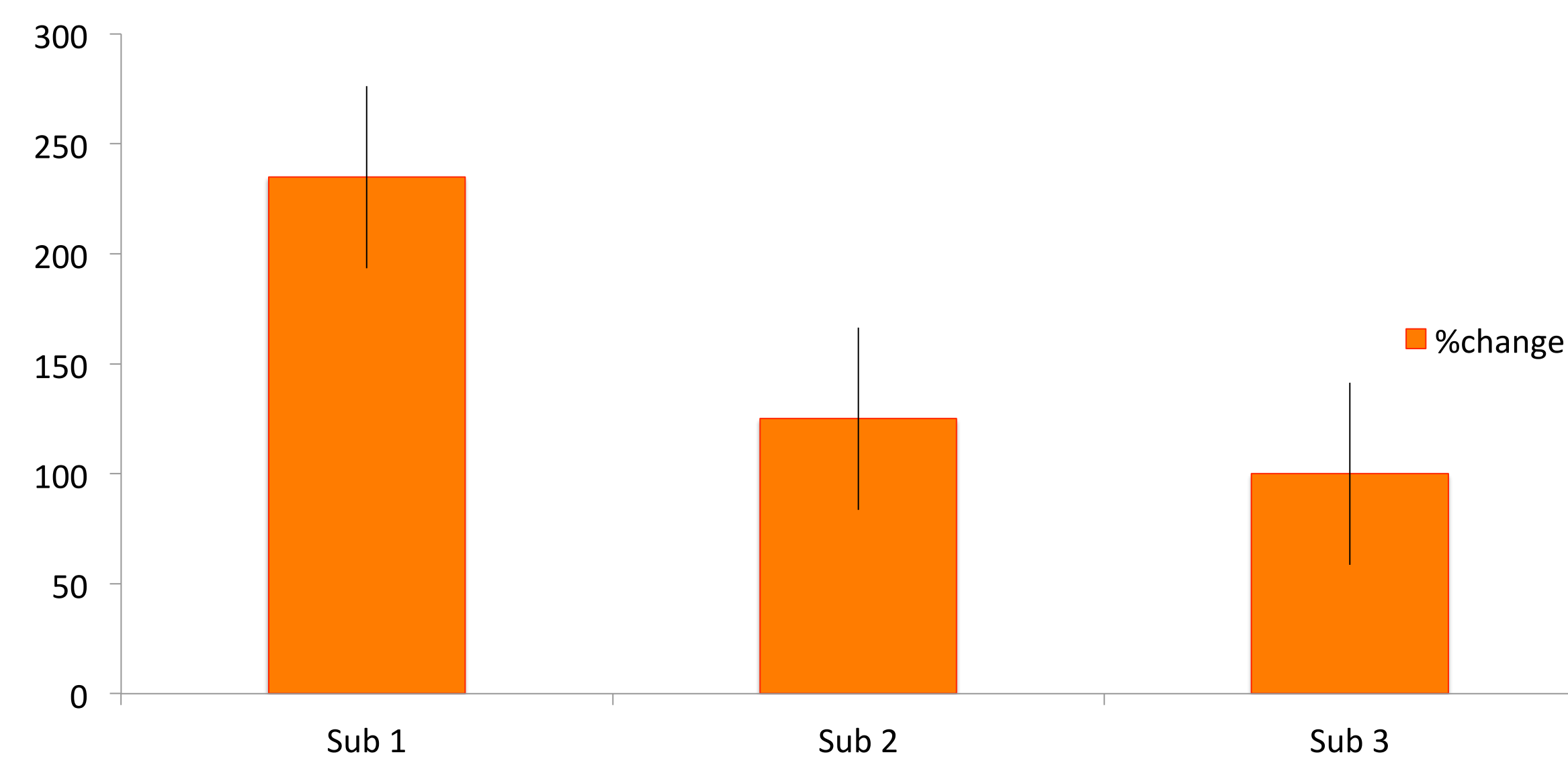


Figure 1: Gamma-NFB Induced change in training threshold from baseline after 8 sessions. S1 showed 234.86% change; S2 showed 125% change; S3 showed 100% change.

Gender Effects: EEG-NFB training threshold change may be influenced by gender.

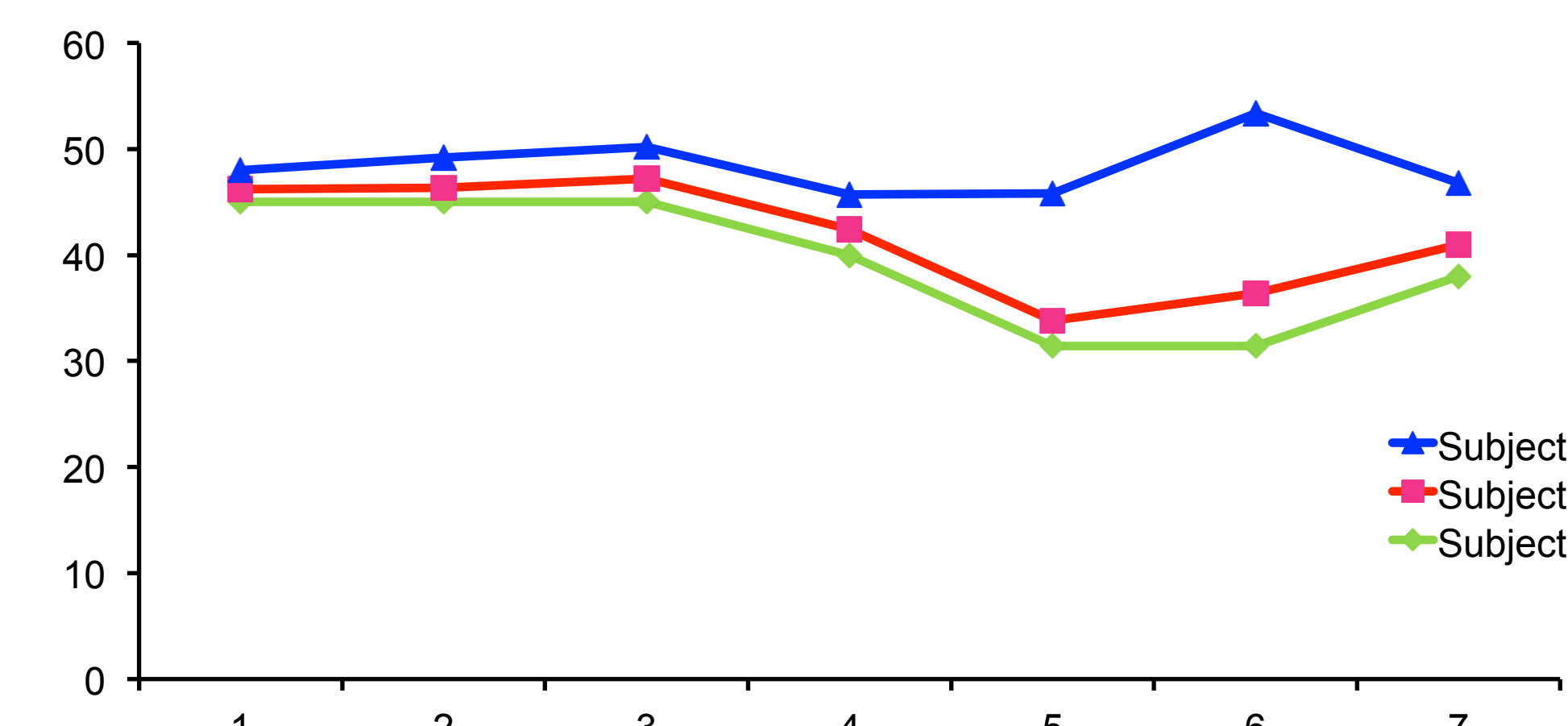


Figure 2: Session by session breakdown of training threshold by subject shows female subject's training threshold plateaus in session 7, whereas, male subjects are increasing threshold.

RESULTS: Evidence of Brain Change

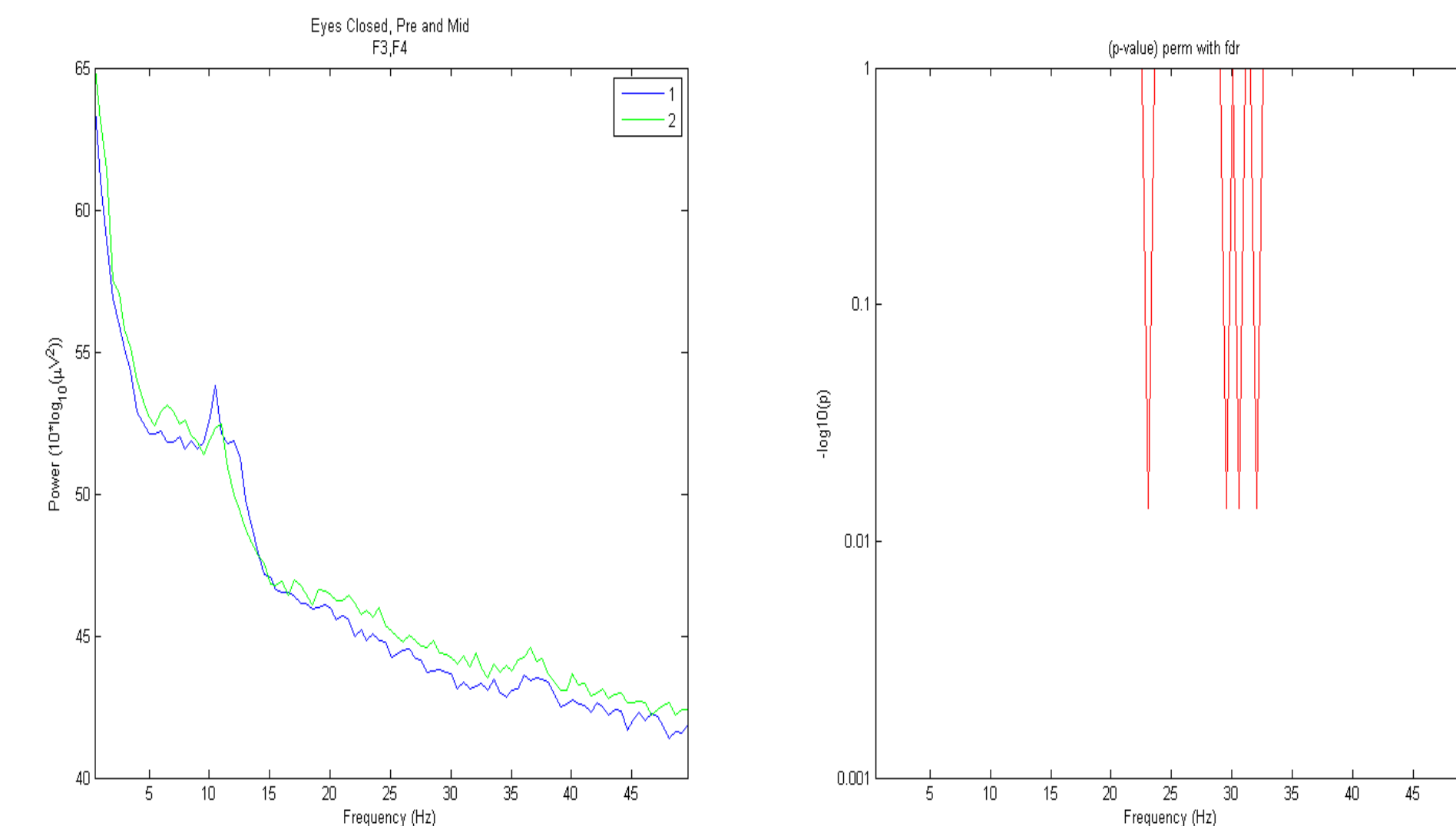


Figure 3: Change in EEG after 4 Weeks of Gamma-Neurofeedback Treatment. Electrodes F3 and F4 in the eyes closed condition, show increase in 20 Hz and 30-35 Hz power ($p < 0.05$).

RESULTS: Changes in Neuropsychological Variables

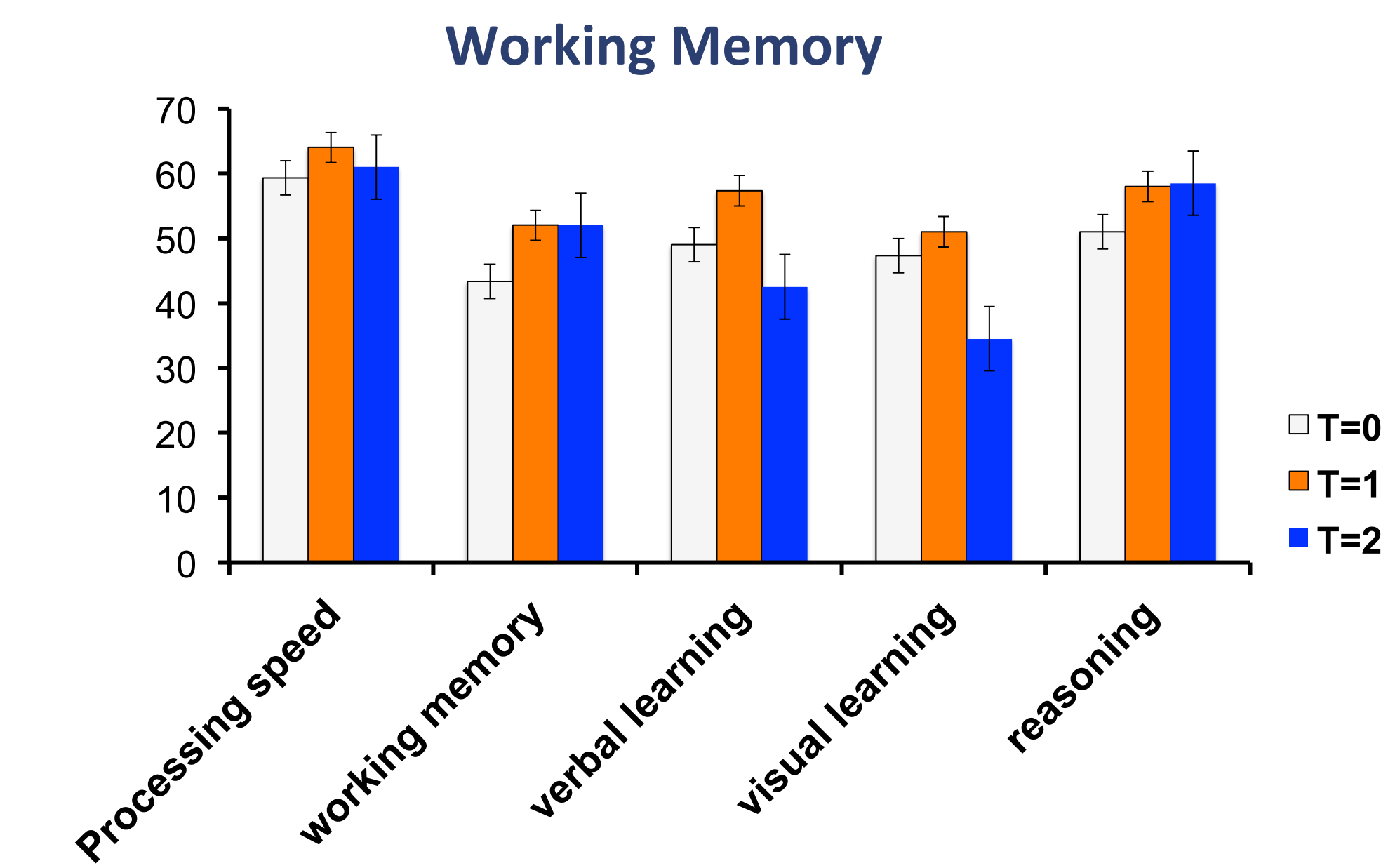


Figure 4: Change in MCCB Scores: All indices increased with gamma-NFB after 8 sessions of training. Gains in Working Memory and Reasoning were maintained after 4 weeks of placebo-training, indicating durability of treatment.

Pretreatment WM and Post-treatment increase in WM are inversely correlated.

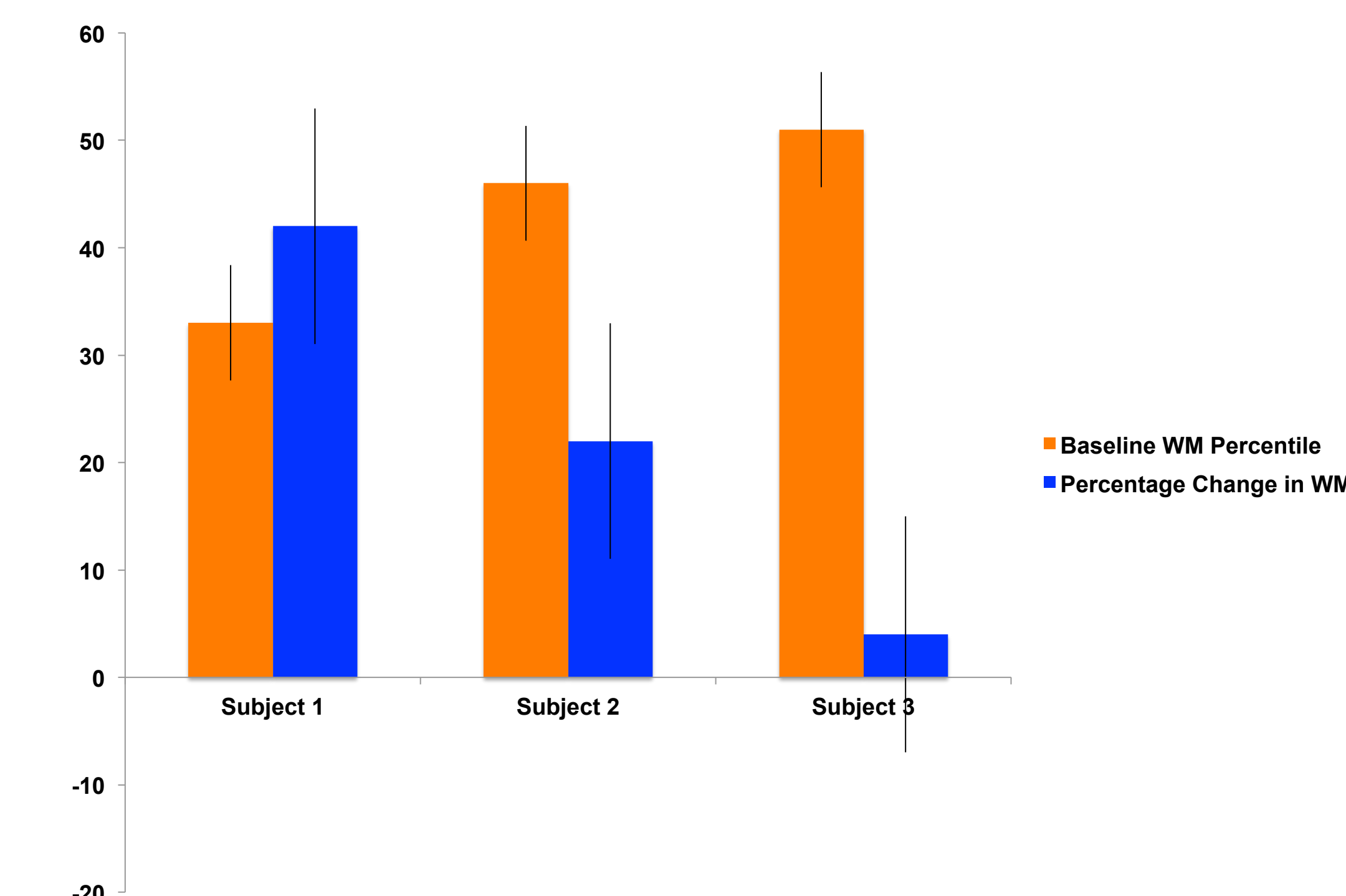


Figure 5: Subject with lowest Pretreatment WM percentile showed the largest gains in WM at post-treatment WM assessment.

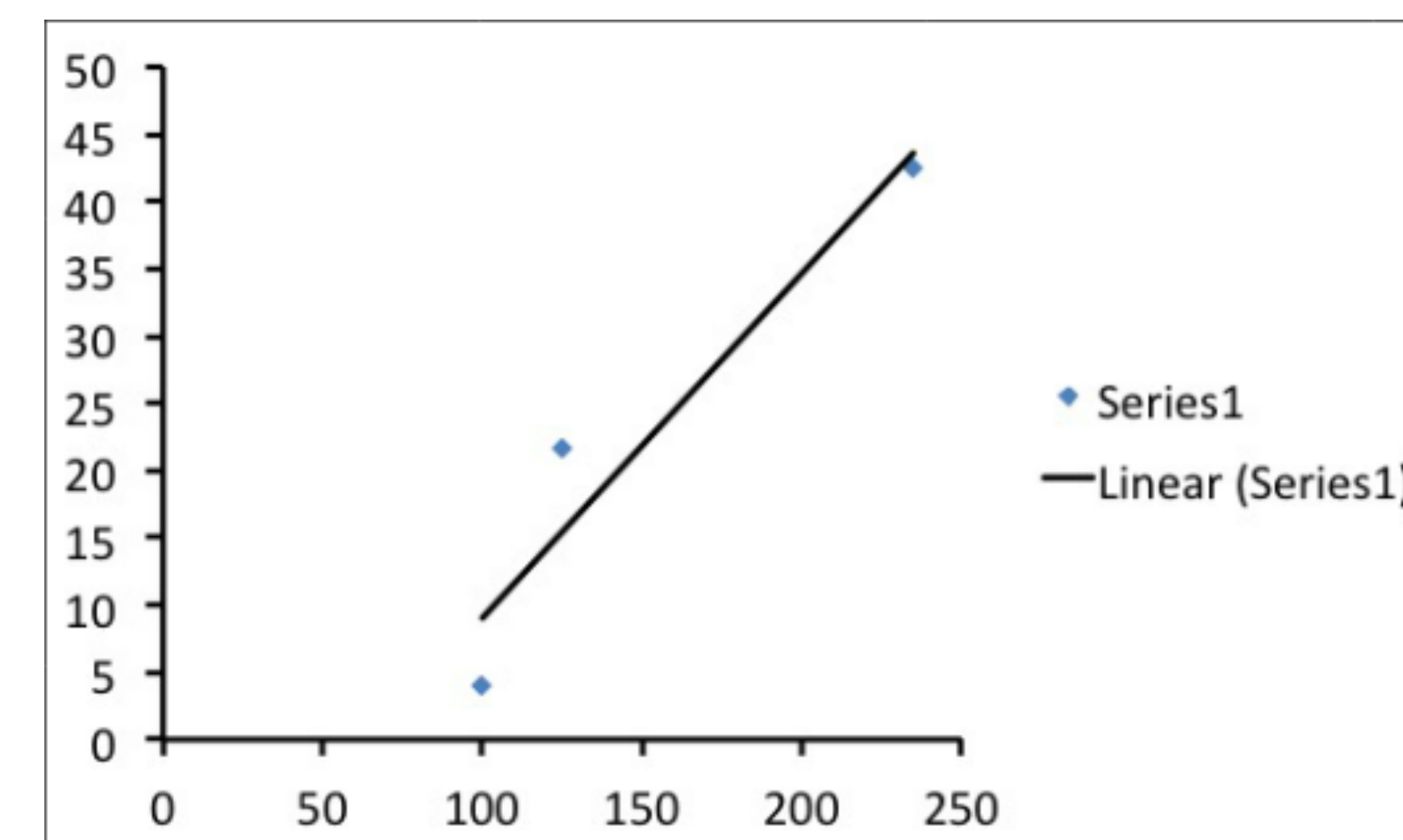


Figure 6: Change in NFB Threshold correlates with change in WM directly. The subject with largest increase in NFB threshold also showed greatest gains in post-treatment WM percentile.

SUMMARY and CONCLUSIONS

- The study was designed as a proof-of-concept study to assess utility of gamma-EEG-NFB to improve WM in SCZ patients.
- Our results provide evidence of a learning effect: All subjects showed increase in training threshold (mean increase of 153%, ranged from 100-235%).
- One female subject showed a slightly altered trajectory of training compared to 2 male subjects.
- Additionally, comparisons between pre and post-treatment EEG showed statistically significant change in gamma power at F3 and F4 electrodes.
- Working memory as measured by the MCCB was increased in all three subjects, and maintained at 4 weeks post completion of treatment.
- Additionally, the subject with the lowest pre-treatment WM percentile gained the greatest increase in post-treatment WM percentile.
- This was further corroborated by a linear, direct relationship between change in training threshold and WM, so that subject with the greatest change in threshold showed the greatest change in WM percentile.
- Average threshold increased during AP-NFB by 66%, but there was no change in WM.
- Thus, the present study indicates that SCZ subjects can undergo NFB to enhance gamma frequency power over the frontal cortices of the brain.
- Enhancements in gamma frequency, but not other frequencies are correlated with improved WM.
- Therefore, the data from this pilot study suggest that NFB may be a successful way to enhance WM and has the potential to be used in a clinical setting to help treat some of the symptoms associated with schizophrenia spectrum disorders.

LIMITATIONS & FUTURE DIRECTIONS

- Small sample size
- Larger study to address gender effects
- Lack of adequate wash-out period before placebo training or 2 groups
- Larger study could also address any treatment order effects, for instance, whether receiving placebo training first, or gamma training impacts overall response.
- We are currently enrolling subjects in a larger study that addresses some of the concerns discussed above.

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