Standardization of EEG Enrichment Marker Acquisitions in a Randomized, Double-Blind, Placebo-Controlled Study of ALTO-300 in Adults with Major Depressive Disorder

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1. Introduction

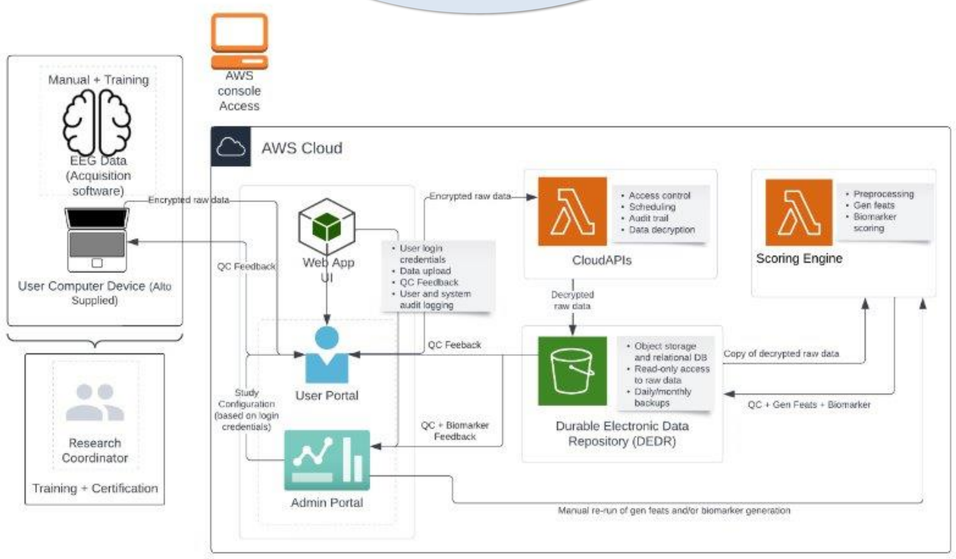
- We present an innovative approach to standardizing the collection of high-quality resting-state EEG (rsEEG) across multiple clinical trial sites. This approach facilitates the use of a reliable EEG enrichment marker for antidepressant response in patients with Major Depressive Disorder (MDD).
- Antidepressants often show little to no differentiation from placebo, likely due to patient heterogeneity within MDD.
- Using biological markers to identify likely drug responders could enhance therapeutic outcomes.
- We analyzed baseline rsEEG data to classify participants as meeting or not meeting the enrichment marker threshold.
- Variability in EEG across sites is a limiting factor for larger trials which we address using a standardized EEG training, data collection, and quality check (QC) approach with real time feedback.
- The study's primary outcome is the efficacy of ALTO-300 versus placebo in reducing MDD symptoms among enrichment-positive participants.

2. Study Design

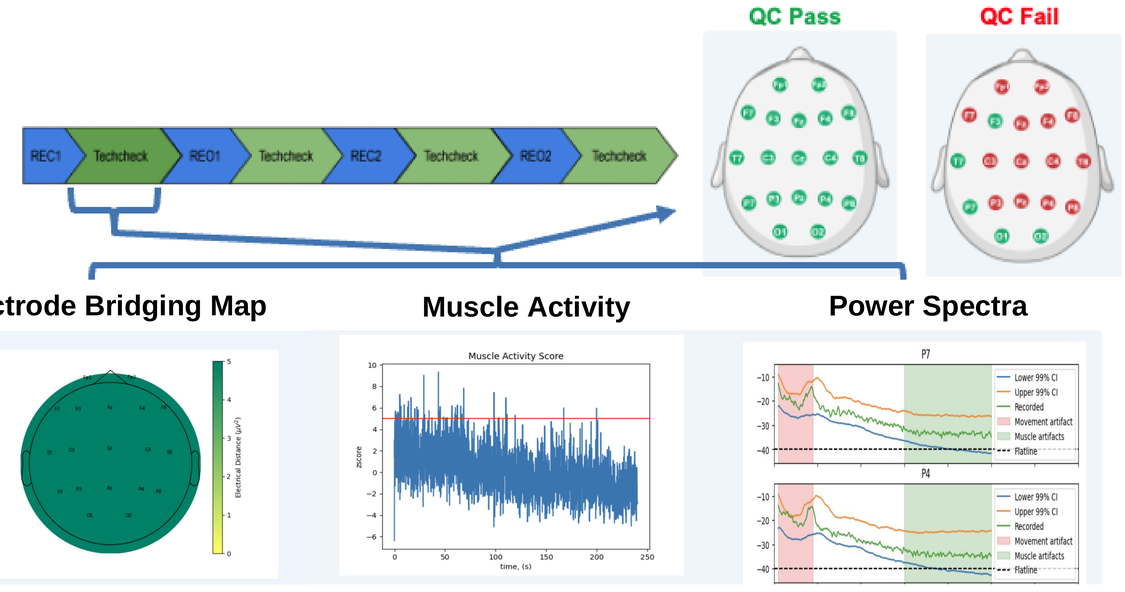
Training
- ✓Onsite Training
- ✓Certification dependent on passing 2 rsEEG test sets
- ✓Standardized documentation
  - ✓User manuals
  - ✓Quick Reference Guides
- ✓Online Support Portal

Equipment
- ✓Standardized EEG systems provided by Alto
- ✓All sites use **same** system, amplifiers, ancillary supplies, standardized operating systems, licenses, data acquisition tools

Ongoing Data Acquisition
- ✓Real Time QC and feedback for uploaded EEG data
- ✓Ability to remotely troubleshoot and deploy updates
- ✓Remotely perform preventative maintenance

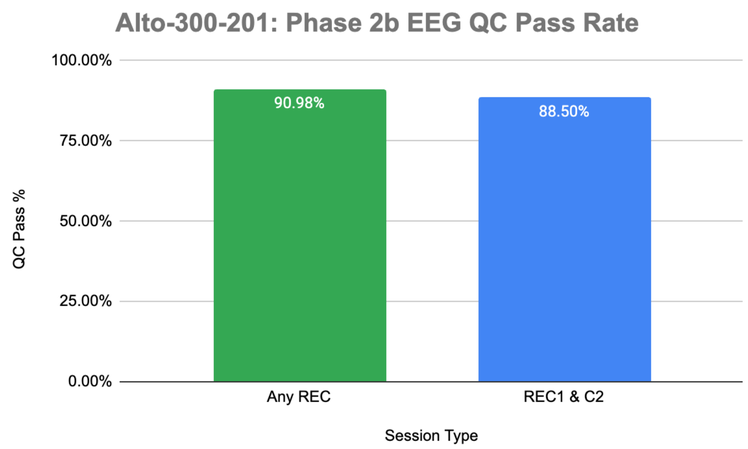


3. Real-time and rapid automated QC feedback:



- Users received automated feedback within 2 minutes of submitting data indicating if a session passed.
- Data was collected with eyes closed & open conditions, each for 4 minutes, repeated twice. At each condition, data had to pass QC before moving to the next run.
- Using proprietary feature generation algorithms, QC-passing data was normalized and compared to threshold values to stratify into either enrichment marker positive or negative group.
- Results were generated within 24 hours and entered in the randomization system.

4. Phase 2b EEG QC Pass Rate



- Trained and Certified > 100 site staff
- 45 + research sites
- Baseline data > 350 participants since start of the study
- 88.5% QC Pass Rate for passing both REC blocks (>90% for passing one of two blocks)

5. Conclusion

- We successfully developed and deployed a standardized EEG data acquisition and analysis platform to collect high quality data across large numbers of clinical trial sites for the purpose of EEG-based patient selection.
- The EEG platform supports a precision psychiatry drug development approach with the goal of identifying participants most likely to respond to treatment with ALTO-300.

6. Acknowledgments

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