Pinpointing Placebo Responders Using Multi-Component Vocal Analysis

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Method

I. *RECORD SPEECH*

1) Twenty subjects randomized to placebo or drug

2) Two minutes of spontaneous speech recorded

3) Prompt: "How do you like to handle your relationships with other people?"

II. *OBTAIN SPECIMENS FOR ANALYSIS*

1) At three weeks, identify placebo treated subjects

2) Extract 20 sec of continuous speech

3) Measure acoustic features-- pitch, intensity, formant frequencies and bandwidths-- per 10msec in the PRAAT.

III. *COMPUTE FEATURE STATS IN MATLAB*

1) Compute simultaneous deltas of acoustic features per 10ms

2) Compute descriptive stats for each pair of features.

3) For paired features , separate the most frequent (core) simultaneous deltas from the less frequent (border)

IV. *COMPARE PLACEBO RESPONDER WITH PLACEBO NON-RESPONDER COMPONENTS*

1) Identify Placebo Responders and Placebo Non-Responders

2) Compute stat ratios, yielding 2809 candidate variables.

3) Perform PRINCIPAL COMPONENT ANALYSIS, reducing variables to those that correlate at >60% with both the Placebo Responder and Placebo Non-Responder Components. Yield=97 variables

4) Perform tests of normality and significance

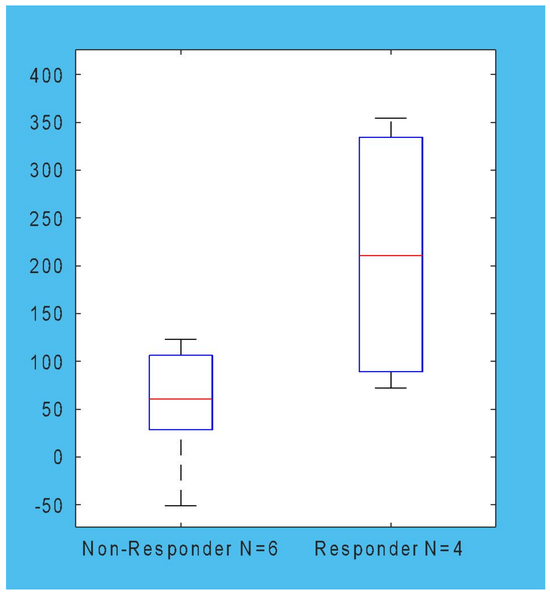
RESULTS

Placebo Responders Have A Distinct Vocal Profile

Placebo Responder (PR) N=4
Placebo Non-Responder(PNR) N=6

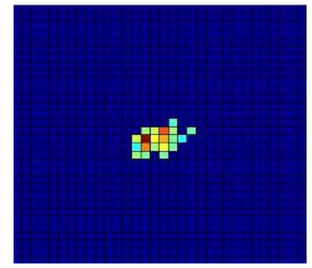
Initial HAMD/MADRAS Mean(SD):
PR mn(SD)= 31.5(2.6)
PNR mn(SD)= 31.8(7.5)

Final HAMD/MADRAS Mean(SD):
PR mn(SD)= 12.3(2)
PNR mn(SD)= 25.8(4.5)

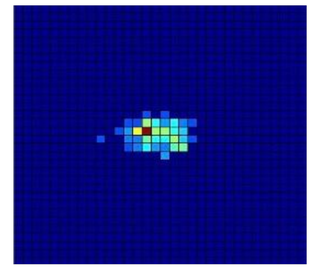


Variable 1 (core) = k/cov(ΔP,ΔI)
mean(SD)PR=154.5 (102.3)
mean(SD)PNR= 39.6 (51.7)
p<.045
Cohen's d=1.42

Variable 2 (border) = k/cov(ΔP,ΔI)
mean(SD)PR=211.8(143.2)
mean(SD)PNR=54.6(62.8)
p<.043
Cohen's d=1.42



NON-RESPONDER



RESPONDER

DISCUSSION

This is a small pilot study. It demonstrates the use of multi-component vocal analysis to identify likely placebo responders prior to a clinical trial. Placebo responders display weaker linkage of pitch and intensity activity relative to placebo non-responders.

The effect size is large, corresponding to a 76% probability of accurately identifying placebo responders.

Repeating this study with a larger N, multiple segments per recording, and machine learning tools will increase predictive precision.

This method, if validated, will reduce trial size and increase the likelihood of obtaining a signal.

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