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

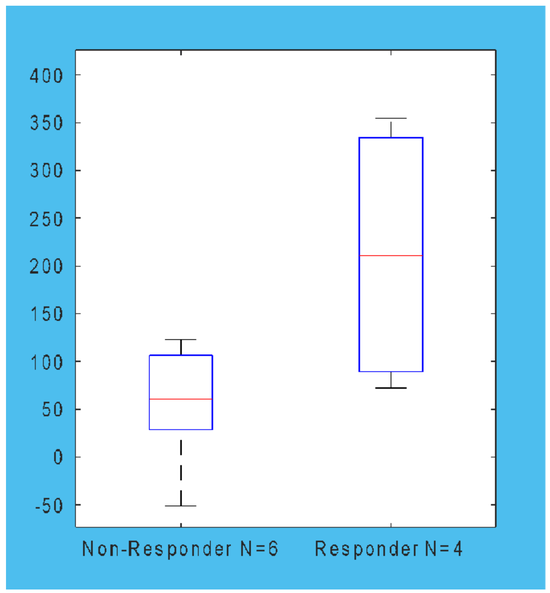
RESULTS

Placebo Responders Have A Distinct Vocal Profile

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

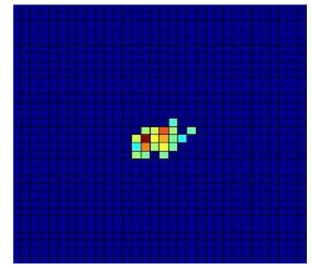
Initial HAMD/MADRS Mean(SD):
PR mn(SD)= 31.5(2.6)
PNR mn(SD)= 31.8(7.5)

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

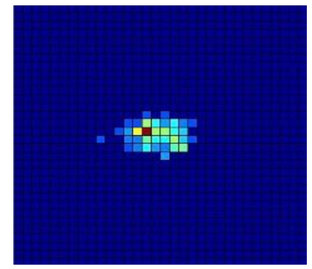


Variable 1 (core) = k/cov(ΔP,ΔI)
mean(SD)PR=154.5 (102.3)
mean(SD)PNR= 39.6 (51.7)
p<.045
Cohen's d=1.42

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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