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Phonological markers of Oxytocin and MDMA ingestion

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Abstract

Speech data has the potential to become a powerful tool to provide quantitative information about emotion beyond that achieved by subjective assessments. Based on this concept, we investigate the use of speech to identify effects in subjects under the influence of two different drugs: Oxytocin (OT) and 3,4-methylenedioxymethamphetamine (MDMA), also known as ecstasy. We extract a set of informative phonological features that can characterize emotion. Then, we perform classification to detect if the subject is under the influence of a drug. Our best results show low error rates of 13% and 17% for the subject classification of OT and MDMA vs. placebo, respectively. We also analyze the performance of the features to differentiate the two levels of MDMA doses, obtaining an error rate of 19%. The results indicate that subtle emotional changes can be detected in the context of drug use.

Index Terms: Phonology, Emotion, Oxytocin, MDMA.

1. Introduction

The effects of psychoactive drugs are generally reported through introspective, subjective measures. However, objective quantitative measures would be a useful addition as they would help to minimize subject evaluation biases and inaccurate self-reports. In recent years, researchers have focused on providing alternative evaluations to be used as an objective tool to aid clinical diagnoses. An ideal source is speech due to its low cost, easy acquisition and high reliability. Current studies have focused on the use of speech to detect a variety of disorders such as Alzheimer's [1], [2] and Parkinson's Disease [3]. In addition, speech has been explored to detect emotional states [4]–[6]. We propose an acoustics-based approach to characterize the effects of two well-known drugs: Oxytocin (OT) and 3,4-methylenedioxymethamphetamine (MDMA).

MDMA, commonly known as ecstasy, is a popular drug in social settings [7]. Following ingestion, large amounts of serotonin are released, causing elevated mood, empathy and emotional closeness [8] and producing effects such as sociability, amicability, and interpersonal closeness [9]–[14].

In the case of OT, commonly known as the "love hormone", studies have also associated this drug with positive emotional valence. Burkett and Young [15] found that the effects of using OT has much in common with the effects of social bonding and attachment. Other researchers have found that OT induces prosocial and affiliative behavior [16]–[18]. Some studies have found that both OT and MDMA are positively correlated with amicability and gregariousness, although there appears to be a stronger correlation with OT than with MDMA [19]. Overall, MDMA and OT have overlapping but not identical effects, as reported in several prosocial effect studies [20]–[22]. Based on this previous work, we focused our analysis on the extraction of acoustic features that can capture these positive emotions.

Prior work has used numerous acoustic features to recognize the emotional content of speech, including prosody, articulation and spectral energy distribution [23], as well as Mel-frequency cepstral coefficients (MFCC) [4], [24]–[27]. For example, in [28], the authors showed that mean values of MFCCs can help differentiate between boredom and neutral emotions, the latter presenting lower mean MFCC values. The position of the formants in the vowel space has also been studied for speech emotion recognition [5], with the finding that formant frequency values are affected by the valence dimension. They found that positive emotions have higher second formant (F2) values. The authors also found a similar trend of high values of F2 and F1 for high arousal.

In this work, we characterize the effects on speech of MDMA and Oxytocin, compared to a placebo, using a set of phonological features as described in the following section. To the best of our knowledge, this is the first attempt to characterize the acoustics of speech in subjects who are under the influence of different drugs. In addition, we evaluate the impact of the extracted features in a classification task to differentiate the effect of the consumption of any of these drugs based on the speech analysis.

2. Methods

2.1 Database

2.1.1 Participants

Participants were recruited under procedures approved by the University of Chicago Institutional Review Board and consisted of 32 healthy subjects: 12 females (F) and 20 males

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(M). The two gender groups were matched by age (F: 24.6 ± 4.7 years, M: 24.1 ± 4.5 years). Exclusion criteria included medical illness, psychiatric disorder, body mass index outside [18.5, 30] kg/m^2, cardiovascular disease, prior adverse ecstasy response, pregnancy and lactancy.

2.1.2 Design and Protocol

Participants received placebo, OT and two doses of MDMA (0.75 mg/kg and 1.5 mg/kg) at 4 different sessions. The order in which participants received the drugs was randomized. Participants were asked to abstain from food consumption for 2 hours; cannabis for 7 days; alcohol or medications for 24 hours; and all other illicit drugs for 48 hours prior to taking each drug. The latter requirement was verified with urine, saliva, and breathalyser tests. In addition, pregnancy tests were administered for female participants. Speech was recorded during the expected peak effect of each drug [35].

2.1.3 Procedure

Participants were asked to speak for five minutes. During each session, the research assistant started the voice recorder and then left the room. Thus, all speech was pure monologue, with no listener. Participants' speech was recorded at 44.1 kHz in WMA format.

2.2 Preprocessing

The initial and final 30 seconds of each 5-minute recording were removed to ensure better reliability of the context of the speech.

2.3 Feature Extraction

Eight different types of features were used to characterize the speech of subjects under placebo, MDMA and OT. The feature set (summarized in Table 1) is described here.

2.3.1 Pitch

Pitch was obtained using the autocorrelation method in Praat software for 40 ms samples [29]. For a better estimation, a Hanning window of 5 ms was used. Since we obtained a pitch distribution for each recording, we extracted 6 types of statistical descriptors. Median and interquartile range (IQR) are used instead of mean and standard deviation to avoid the effect of outliers. Then, we extracted the 5th (pct5) and 95th (pct95) percentile values to represent minimum and maximum estimates and the 3rd and 4th moments (skewness and kurtosis) to characterize the shape of the distribution.

2.3.2 Vowel space

Changes in the formant distribution have been associated with changes in emotion [5]. Therefore, we also extracted features from the formant space. First, we extracted the vowels for each recording using a Praat plug-in; details can be found in [30], [31]. Then, for each frame, we applied a pre-emphasis filter at 50 Hz, and extracted 5 formants, setting the maximum formant frequency to 5000 and 5500 Hz for males and females, respectively. Although 5 formants were extracted, we only analyzed the values of the first three (F1, F2 and F3). In addition to calculating the formant values, we also extracted the information of the bandwidth of each of the formants (B1, B2, B3). Since these features were extracted in 25 ms-wide windows from the 4-minute speech recording, we calculate the median, IQR, pct5, pct95, skewness and kurtosis for each formant and their bandwidth information. To complement these features, we also compute the orientation (angle) of the distribution of samples in the vowel space (F1 vs. F2) to find if there was a rotation of the vowel space given the use of different drugs.

2.3.3 Long Term Average Spectra (LTAS)

Changes in the LTAS have been shown to be a significant marker of improvement after voice therapy [32]. For this work, we computed the LTAS for the entire 4-minute speech sample. To characterize the spectra, we computed the slope of the energy, the energy at the highest peak and its corresponding frequency value. We also computed the median and the IQR of the energy.

2.3.4 Pause duration

Speech is not a continuous barrage of acoustic energy; rather, speakers pause between syllables and words. We detected and extracted duration of pauses, using the following parameters: silence threshold of -25 dB, minimum duration of 100 ms, and minimum pitch 75 Hz. To characterize the distribution, we extracted median, IQR, pct5, pct95, skewness and kurtosis.

2.3.5 Sounding duration

We also measured the duration of words produced by the speaker, with pauses removed; namely, the duration of sound produced when the speaker was speaking. Again, we extracted median, IQR, pct5, pct95, skewness and kurtosis.

2.3.6 Syllable Nuclei

To characterize speech rate, we used the method proposed by Jong et al. in [33]. We estimated the number of syllables in each recording and used that to compute two features: speech rate (number of syllables over the 4 minutes of recording), and articulation rate (number of syllables over the 4 minutes of recording after pauses were removed).

2.3.7 Spectral Flatness

This feature characterizes the audio spectrum by looking at its shape. It has been previously associated with different emotional states [34]. Spectral flatness is a ratio of the geometric mean and arithmetic mean of the power spectra.

2.3.8 Mel Frequency Cepstral Coefficients (MFCCs)

Sixteen MFCCs were calculated as suggested in [3]. The values were estimated for windows of 25 ms with 10 ms overlap. We computed the median value and IQR for all the coefficients calculated over 4 minutes of recording and used those values as features.

Table 1: Summary of all features

Feature Number	Description
1-6	Pitch
7-43	Vowel space features
44-48	LTAS
49-54	Pause duration
55-60	Sounding duration
61-62	Syllable nuclei
63	Spectral flatness
64-95	MFCCs (16)

2.4 Statistical analysis

A total of 95 phonological features were extracted from each recording. To evaluate if the features can provide some insight into how the tested drugs affect the speech acoustics, we performed Wilcoxon signed-rank tests because we cannot assume a normal distribution for each feature. In addition, we performed a false discovery rate (FDR) correction at $q<0.05$ to correct for multiple comparisons.

2.5 Classification

The main purpose of this analysis was to see if we can differentiate the effects of each drug from placebo. To evaluate the potential of these features, we calculate the performance of the 6 possible binary classification tasks. Since drug and placebo effects were measured in the same pool of subjects, our analyses were conducted on the within-subject drug effects normalized to the baseline. For example, to classify placebo vs. OT, we classify placebo-OT vs. OT-placebo. In this way, any irrelevant inter-subject differences (e.g. pitch in women is generally higher than in men) was subtracted out.

After feature standardization (mean = 0 and standard deviation = 1), we perform a two-sample t-test to rank our features. Then we select the subsets of the most informative features and apply 7 classifiers, which are specified in Table 4. The classification performance was estimated via a leave-one-subject-out cross-validation approach, its parameters being selected via an internal 5-fold cross-validation. In other words, a nested cross-validation scheme was used to calculate classification error rates and optimal parameters.

3. Results & Discussion

3.1 Statistical analysis

Table 3 shows the top 5 features with lowest p-value obtained for the paired comparison between placebo and the three drug categories. We observe that for OT the *p*-values are lower than for MDMA features. This indicates that there is higher divergence from placebo in the phonological elements of speech for participants under the influence of OT compared to MDMA. We also observe that most of the features with low *p*-value and especially those that pass FDR correction (marked by * in Table 2) are related to changes in F2. When we look at the sign direction, we find that the values of F2 were higher for OT than for placebo. This correlates with prior work of Goudbeek et al. [5], showing that positive valence (elation, pleasure, etc.) resulted in higher F2 values. Our findings also indicate that the variability of F2 (IQR F2) decreases for subjects under the influence of OT. This can be seen by looking at the distributions of IQR values shown in the bottom row of Figure 1. This difference is very strong for OT, though it can also be observed for the two doses of MDMA (higher change at 1.5mg/kg). Previous research in formant information to detect emotion [24] showed an association between low F2 variability and subjects expressing happiness. This means that positive changes of mood are captured by this feature.

One of the phonological features that showed a significant difference between placebo and MDMA 0.75mg/kg is pitch (see Table 2 and Figure 1): Participants' speech was pitched lower when they were using MDMA as compared to placebo. The same numerical trend is observed for OT, but the difference did not pass the FDR correction (*p*-value = 0.03). At the higher dose of MDMA (1.5 mg/kg), this significant difference of pitch between the drug and placebo conditions disappears (*p*-value = 0.34), although there is a slight numerical increase in pitch compared to placebo, especially at higher pitch values (likely in female subjects). The potentially differing effects of psychoactive drugs on men and women should be further evaluated in future studies. Overall, the significance is lower for placebo vs. MDMA 1.5mg/kg with only 3 features with *p*-value < 0.05, none of them passing FDR correction. We observe that the most significant is the median of MFCC #12. When we analyze the distribution of the values, we observe that the values of the coefficient are higher for subjects under placebo.

Table 2: Wilcoxon signed rank test results (top 5)

Category	*p*-value	Feature Description
MDMA (0.75mg/kg)	5.23E-4*	Median pitch
	1.74E-3	Percentile 5 pitch
	1.11E-2	IQR MFCC #13
	1.32E-2	Percentile 95 pitch
	1.71E-2	Percentile 95 B3
MDMA (1.5mg/kg)	6.5E-3	Median MFCC #12
	2.20E-2	Percentile 5 F3
	2.42E-2	Percentile 5 B2
	6.28E-2	Kurtosis B1
	6.28E-2	IQR pause duration
Oxytocin	2.75E-4*	Kurtosis F2
	8.45E-4*	IQR F2
	2.86E-3	Kurtosis B1
	3.22E-3	Skewness B1
	4.35E-2	Percentile 5 of F2

3.2 Classification Results

Table 3 summarizes our classification results for each of the 6 combinations of placebo, MDMA 0.75 mg/kg, MDMA 1.5 mg/kg, and OT. We observe that the lowest classification error is obtained when OT is compared to placebo, regardless of the classifier being evaluated. The lowest error is obtained for nearest neighbor (error rate 0.13).

We also calculated the area under the ROC curve (AUC) shown in Fig. 2 obtaining 0.92. This is consistent with our prior statistical analysis, where more informative features were found for OT vs. placebo. In the case of MDMA 0.75mg/kg vs. placebo a low error rate of 0.17 (AUC = 0.81) is achieved with Random Forests. For this category, other classifiers have good performance too. However, when placebo is compared with MDMA 1.5mg/kg, the error rate is between 0.31 and 0.38. Despite being higher than chance probability, these results may be related to the fact that sex may have a different response in MDMA in higher doses.

When we perform classification to differentiate between the two levels of MDMA, we obtain a low error rate of 0.19. This could mean that a higher dose of 1.5mg/kg can change speech effects in a reversed direction. For example, pitch becomes lower for the low dose but when the dose increases, we observe that the pitch starts becoming slightly higher in comparison with the lower dose, though the difference is not significant compared to placebo. Effects of MDMA at a yet higher dose need to be investigated to see if pitch increases even more.

Overall, the number of features used to obtain the best

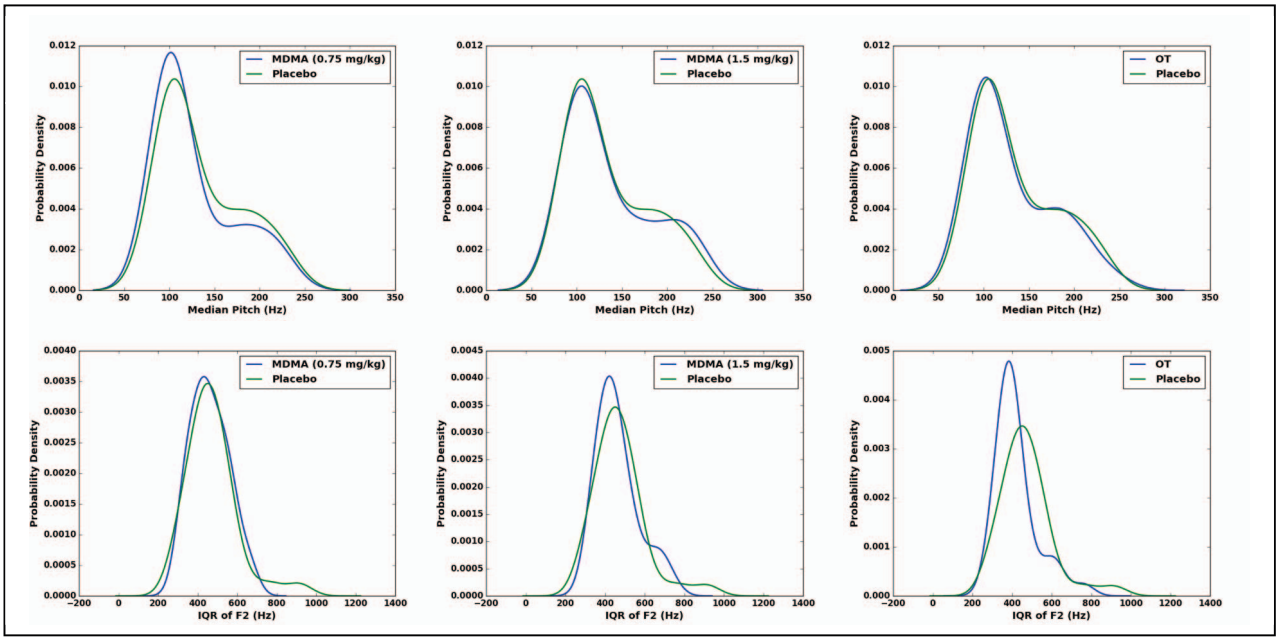

Figure 1: Comparison of distributions between drugs and placebo for: Median pitch (top row) and IQR F2 (bottom row).

Table 3: Error rate for each comparison and classifier, with the optimal number of features listed in parentheses. Bolded values show the classifier with the lowest error rate.

Classifier	PBO vs. MDMA 0.75	PBO vs. MDMA 1.5	PBO vs. OT	MDMA 1.5 vs. MDMA 0.75	OT vs. MDMA 0.75	OT vs. MDMA 1.5
Logistic Regression	0.22(5)	0.34(3)	0.22(5)	**0.19(3)**	0.31(3)	0.38(50)
Nearest Neighbors	0.36(3)	0.34(all)	**0.13(5)**	**0.19(3)**	**0.25(5)**	**0.28(60)**
Naive Bayes	0.34(3)	**0.31(3)**	0.16(10)	**0.19(3)**	0.31(3)	0.34(10)
Lasso	0.25(5)	0.38(3)	0.19(5)	0.25(3)	0.31(3)	0.38(80)
Linear SVM	0.32(3)	**0.31(3)**	0.19(5)	0.22(3)	0.28(3)	0.34(50)
Elastic SVM	0.25(70)	0.34(3)	0.16(5)	0.25(3)	**0.25(3)**	0.31(60)
Random Forest	**0.17(15)**	0.33(3)	0.19(20)	0.23(3)	**0.25(3)**	0.30 3)

results are low except for OT vs. MDMA 1.5mg/kg, where a higher number of features is required to obtain a better performance. This finding may be attributed to the high variability in MDMA 1.5mg/kg.

4. Conclusions

We present the first study that uses acoustic characteristics of speech to identify the presence and type of drugs. The most relevant features correlate with positive valence, which supports previous research of drug effects using subjective analyses.

Recent work conducted by some of our co-authors on a reduced dataset [37] found that the semantic analysis in speech can differentiate when a participant is under the influence of a placebo vs. MDMA. Our next step is to integrate both modalities (semantic and acoustic analysis) to find complementary features that can help achieve a higher differentiation between the categories.

Our results suggest that phonological features may be a potential future solution to replace subjective analyses to improve the reliability of the clinical studies for drug effects assessments. For future work, we plan to correct the effects of sex as well as incorporate semantic analysis to further improve our results.

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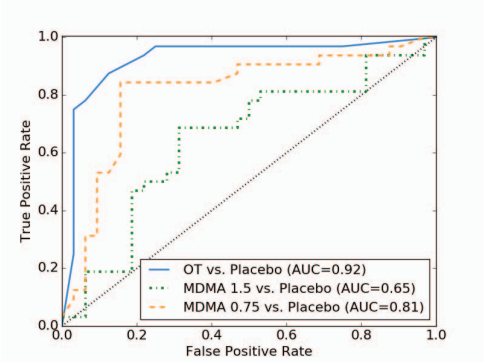

Figure 2: ROC curves for the best performance classifiers (see Table 3) between placebo and different drugs.

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