

Predictors of Effect of Atypical Antipsychotics on Speech

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ABSTRACT

Background: Most of the studies have looked into the effect of typical antipsychotics on speech secondary to tardive dyskinesia. **Aims:** This study was aimed to explore the factors predicting the effect of atypical antipsychotic medications on the production of speech. **Materials and Methods:** One hundred and forty patients on stable regimen of three or more months on risperidone (92), olanzapine (28), aripiprazole (14), and clozapine (6) were recruited for the study. Speech was assessed by maximum phonation duration task, s/z ratio, diadochokinetic task, acoustic analysis and Frenchay Dysarthria Assessment (FDA). Extrapyramidal symptoms (EPS) were assessed by Simpson Angus scale. **Statistical Analysis:** Spearman correlation analysis was carried out to find the association between speech parameters and continuous variables. Effect of EPS, duration and dose of antipsychotic treatment on speech parameters was compared using Mann-Whitney test. **Results:** The risperidone group differ from other antipsychotics groups significantly in s/z ratio (0.07), FDA-total (0.23) and FDA-reflex (0.25). People who took antipsychotic for more than 2 years had lower score of FDA-palate ($P = 0.042$), and FDA-respiratory ($P = 0.04$) and higher values in noise-harmonic ratio ($P = 0.011$) and maximum fundamental frequency (MFF) for males ($P = 0.02$). Effect of EPS was seen on MFF for males (spearman correlation coefficient = 0.34) and on almost all sections of FDA (spearman correlation coefficients = -0.2 to -0.33). **Conclusion:** Both duration of use and propensity of atypical antipsychotics to cause EPS can influence the speech performance of the patients. This information can be useful, particularly in people with the requirement of high quality speech.

Key words: Atypical antipsychotics, dysarthria, extrapyramidal symptoms, maximum fundamental frequency, noise-harmonic ratio, s/z ratio, speech

INTRODUCTION

Antipsychotic drugs can influence the neuromuscular system, and hence have the potential to affect speech production mechanism. Speech problems

particularly acquired type can have a negative impact on communication and life-experiences.^[1] So far, most studies have focused on typical antipsychotics which again, is limited to cases who had tardive dyskinesia

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(TD) and tardive dystonia.^[2] The literature on speech difficulties with atypical antipsychotics are only available as anecdotal reports and commonly implicated atypical antipsychotic drugs affecting speech production are risperidone, olanzapine, and clozapine. The speech problems reported were speech dysfluency or stuttering, and dysphagia.^[3,4] The other speech subsystems such as respiration, phonation, and objective voice analysis are not studied in patients with atypical antipsychotics.

Speech is affected in Parkinson's disease (PD) in all its stages across the various dimensions of speech production. It includes voice quality, breathing, articulation and prosody of speech.^[5] Parkinsonism symptom or extrapyramidal symptoms (EPS) is an adverse effect of antipsychotics including atypical ones^[6] and may influence speech production of patients on atypical antipsychotics. Besides, the effect of other characteristics of antipsychotic treatment on speech production needs to be determined.

This study was planned with the aim to examine the pattern of speech production in patients who are stabilized on atypical antipsychotics and find the associated treatment variables as predictors of associated speech problems if any.

MATERIALS AND METHODS

Subjects

A total of 140 patients in the age range of 20-60 years (mean age = 35.9 years, standard deviation [SD] = 10.9 years) were recruited. Eighty-one (57.9%) were males and 59 (42.1%) were females. They were diagnosed as either schizophrenia (67 patients, 47.9%), persistent delusional disorder (17 patients, 12.1%), or acute and transient psychotic disorder (56 patients, 40%) as per the International Classification of Diseases-10 classification of mental and behavioral disorders^[7] and were on the stable regimen of one of the following antipsychotics for a minimum duration of 3 months-risperidone/olanzapine/clozapine/aripiprazole. For the convenience of nomenclature, the dose of antipsychotic was considered low if it was ≤ 4 mg/day for risperidone, ≤ 10 mg/day for olanzapine, ≤ 15 mg/day for aripiprazole, and ≤ 200 mg/day for clozapine. Doses greater than this were considered to be high. The only psychotropic medications allowed concurrently were benzodiazepine and trihexyphenidyl.

Patients having TD as mild or more degrees of movements in any area according to abnormal involuntary movement scale^[8] were excluded. The presence of tardive dystonia was also an exclusion criteria. Those having co-morbid illnesses, which are likely to cause speech difficulties were also not recruited. None of them had a history of speech

difficulty before the starting of an antipsychotic drug. They were either Kannada, Hindi or English speaking and gave written informed consent for their participation in the study. The study was approved by the Institute's Ethics Committee. The investigator examining the speech performance was fluent in Kannada, Hindi and English languages.

Procedure

The assessments were done in a single visit. The respiratory and laryngeal (glottal sufficiency) subsystems were assessed by maximum phonation duration (MPD) task and s/z ratio. The MPD task measures the time till the individual sustains a vowel sound (here /a/) produced in one deep breath at a relatively comfortable pitch and loudness. s/z ratio takes the ratio of time for consonant /s/ to that of consonant /z/. In both tests, the best of three attempts at sustaining the vowel was considered.^[9]

Diadochokinesia (DDK) represents the ability of repeating a simple segment of speech at maximum speed.^[10,11] The iterations per second was noted for rapid repetition of a single syllable (/pa/, /ta/, or /ka/) and a syllable sequence (/pataka/). The former is called alternate motion rate, and the latter is called sequential motion rate.

The objective acoustic analysis of voice was done by multidimensional voice profile in the computerized speech laboratory- 4300 (Kay Elemetrics) software. We assessed the sustained vowel phonation (/a/) in the middle phase of 3 s discarding at least the first 25 ms of phonation, as well as the terminal phase of phonation. In this study, voice parameters analyzed were maximum fundamental frequency (MFF) (in Hertz), jitter (%), shimmer (%), and noise to harmonic ratio (NHR), which represent the fundamental frequency, frequency perturbation, amplitude perturbation and noise related aspects of voice, respectively.^[12] The average of two attempts was measured.

We administered the Frenchay Dysarthria Assessment (FDA), FDA-2nd Edition^[13] to assess oromotor involvement and dysarthria. FDA includes seven sections that comprise of subsections of reflex, respiration, lips, palate, laryngeal, tongue, and intelligibility. Assessments were carried out for each of these sections by observing the person at rest and while various actions were carried out (such as the swallow, cough, movements of lips and tongue, and variations in speech). Each item within the section was rated on the 10-point rating scale (0-9), and total score for each section, as well as the final score was calculated by averaging them. A detailed evaluation was planned for those speech production or related aspects (like

stuttering or dysphagia) if reported by the patient or detected during history taking.

The presence of EPS, if any, and its degree was assessed using the Simpson Angus scale (SAS).^[14] It has 10 items, which includes tremors, rigidity, bradykinesia (slowness in activity) and postural instability. Each item is rated using a 5-point scale (0-4). The mean score is obtained by averaging the score of all items. The cut-off for antipsychotic-induced EPS was kept as the mean score of 0.65.^[15]

Statistical analysis

Descriptive analysis was done for demographic, clinical and speech-related variables. Spearman correlation analysis was done to find the association between speech parameters and continuous variables (age, duration of treatment with antipsychotic in months and SAS EPS scores). The groups based on the presence of EPS, duration of treatment with antipsychotic medication for more or less than 2 years, and high or low dose of antipsychotic medications were compared separately for various speech parameters using Mann-Whitney test. For MFF, data of males and females were analyzed separately parameters were considered to be significant at $P < 0.05$ level.

RESULTS

Medication details

Ninety-two patients (65.7%) were on treatment with risperidone, 28 patients (20%) on olanzapine, 14 (10%) on aripiprazole, and six (4.3%) on clozapine. The average duration of treatment with antipsychotic was 22.9 months (SD = 33.7 months). Among them, 22 patients (15.7%) were taking the antipsychotic drug for more than 2 years and rest 118 (84.3%) had antipsychotic for two or less than two years. The dose of antipsychotic was high in 51 patients (36.4%) and low in 89 (63.6%) patients. The concurrent medication to antipsychotic was trihexyphenidyl alone in 87 patients (62.1%), and both trihexyphenidyl and clonazepam in 15 patients (10.7%). Thirty-eight patients (27.2%) patients were receiving antipsychotic alone.

Speech parameters

Table 1 shows the mean scores with SDs of speech assessments for 140 patients. On comparing the groups of risperidone and other antipsychotics in *t*-test, the significant difference was noted in s/z ratio, FDA-total score and FDA-reflex [Table 2].

Findings of spearman correlation analysis are presented in Table 3. The values were correlating with SAS mean score for all sections of FDA except palate. The duration of treatment correlated with MFF (for males), FDA-lips

and FDA-reflex. MPD, s/z ratio, DDK, and the acoustic parameters (besides MFF) did not correlate with SAS score or duration of treatment with antipsychotic.

The results of Mann-Whitney test [Table 4], indicates that the group with antipsychotic-induced EPS ($n = 20$) had significantly lower scores for larynx, tongue, intelligibility sections, and total score of FDA and higher values for MFF (in males only) and NHR compared to that in the group without antipsychotic-induced EPS ($n = 120$). Besides, the scores of the palate and respiratory sections of FDA were lower, and MFF (in males only) and NHR had higher values in those who took antipsychotic for longer than 2 years [Table 4].

Table 1: Mean and SD of scores of speech parameters

Speech parameter	Mean (SD)	Speech parameter	Mean (SD)
MPD (s)	10.81 (3.74)	FDA-total score	8.30 (0.47)
S/z ratio	1.19 (0.20)	FDA-reflex	8.40 (0.69)
DDK-AMR (s)	4.59 (0.81)	FDA-respiratory	8.32 (0.69)
DDK-SMR (s)	6.61 (1.05)	FDA-lips	8.20 (0.58)
Jitter (%)	1.92 (2.25)	FDA-palate	8.81 (0.33)
Shimmer (%)	3.58 (2.33)	FDA-larynx	7.95 (0.77)
Noise to harmonic ratio	0.14 (0.08)	FDA-tongue	8.18 (0.69)
MFF (Hz)			
Males	129.89 (19.61)	FDA-intelligibility	8.70 (0.44)
Females	218.1 (33.70)		

*MPD – Maximum phonation duration; DDK – Diadochokinesia; AMR – Alternate motion rate; SMR – Sequential motion rate; MFF – Maximum fundamental frequency; FDA – Frenchay dysarthria assessment; SD – Standard deviation

Table 2: Speech parameters showing significant difference between risperidone and other antipsychotics

Speech parameter	Mean (SD)		P
	Risperidone group	Other antipsychotic group	
S/z ratio	1.21 (0.22)	1.14 (0.13)	0.030
FDA-total score	8.36 (0.37)	8.59 (0.61)	0.042
FDA-reflex	8.31 (0.72)	8.56 (0.60)	0.034

FDA – Frenchay dysarthria assessment; SD – Standard deviation

Table 3: Spearman correlation analysis for speech parameters and treatment variables

Treatment variable	Speech parameter	Correlation coefficient	P
SAS mean score	FDA-total score	-0.299	<0.001
	FDA-reflex	-0.239	0.004
	FDA-respiratory	-0.194	0.022
	FDA-lips	-0.219	0.009
	FDA-larynx	-0.191	0.024
	FDA-tongue	-0.329	<0.001
	FDA-intelligibility	-0.214	0.011
	MFF-(males)	0.336	0.003
Duration of antipsychotics	FDA-reflex	-0.179	0.041
	FDA-lips	-0.181	0.032
	MFF-(males)	0.292	0.008

*FDA – Frenchay dysarthria assessment; SAS – Simpson angus scale; MFF – Maximum fundamental frequency

Table 4: Significant results of Mann–Whitney test for groups based on treatment factors

Treatment factor	Speech parameter	P
Antipsychotic induced EPS	NHR	0.046
	FDA-total	0.027
	FDA-larynx	0.006
	FDA-tongue	0.025
	FDA-intelligibility	0.012
	MFF-(males)	0.007
Antipsychotic duration with grouping at 2 years	FDA-palate	0.042
	FDA-respiratory	0.040
	NHR	0.011
	MFF-(males)	0.020

*FDA – Frenchay dysarthria assessment; MFF – Maximum fundamental frequency; EPS – Extrapyramidal symptoms; NHR – Noise to harmonic ratio

There was no significant difference in performance in various speech assessments in groups with high and low doses of antipsychotics.

DISCUSSION

This study looked into aspects related to speech performance of patients on atypical antipsychotics. This is the first study of its kind addressing this issue. We assessed various subsystems of speech production, which included respiratory, laryngeal, and articulatory subsystems. In addition, the presence or absences of any other associated speech problems were identified through detailed history.

Patients on different atypical antipsychotic drugs showed similar performance in tests assessing speech production subsystems, albeit few exceptions. Individuals who were on risperidone had increased s/z ratio, and total score and reflex section of FDA, compared to those who were on olanzapine, clozapine or aripiprazole, which may be indicative of the possible effect of risperidone on speech subsystems. In fact, there are case reports of risperidone related dysphagia.^[4,16-18] However, it is noticeable there were additional factors in these cases such as tardive dystonia, concurrent medication (lithium), intellectual disability, or old age, which would have had a confounding effect in addition to medication.

EPS associated with the use of atypical antipsychotic drugs can indirectly affect speech production. SAS was used to assess the severity of EPS, and it was found to correlate with the total score, as well as various subsections of FDA which includes the laryngeal, respiratory, articulation, reflex, and intelligibility aspects of speech. Among them, those who had EPS differed in objective analysis of voice from those who do not have EPS. Patients who had EPS symptoms had

higher NHR. MFF was higher in men with increased EPS alone. In fact, literature has reported that in PD, where EPS is the hallmark, the person may have breathy voice quality, reduced pitch, and loudness variation, slurred speech and speech rate problems.^[5,19,20]

Besides EPS, the duration for which the person used the antipsychotic also had an effect on speech parameters, including subsections of FDA, which assessed swallowing, respiration, and articulation. Those who had antipsychotic for more than 2 years had harsh voice and increased fundamental frequency, particularly in men. The mechanisms involved in the long-term effect of atypical antipsychotic on speech require further exploration. The results of this study indicate that it may be beyond the influence of TD and dystonia.

We found statistical significance mostly in parameters of voice. However, these were not clinically or perceptually evident. These parameters may be early markers of speech involvement and needs to be further explored. Another factor to be considered while interpreting the results is that there was an unequal distribution of various atypical antipsychotic drugs in different groups, and hence generalization is difficult. Furthermore, the duration of antipsychotic drug use was variable in the patients recruited in this study. It was a cross-sectional study and hence absence of deficits in the speech production before the start of antipsychotics could be ascertained through history only. The assessor was not blind to the medication status.

CONCLUSION

Atypical antipsychotics can have an impact on speech production independent of TD and dystonia. Some of these effects may be related to the duration of antipsychotics, and some may be linked to the degree of EPS. A prospective study addressing the premedication speech status, as well as follow-up speech evaluation at regular intervals may throw more light in this regard.

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Conflicts of interest

There are no conflicts of interest.

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