Autonomic Nervous System Imbalance in Young Adults with Developmental Stuttering

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ÖZET: Gelişmsel kekemeliği olan genç yetişkinlerde otonom sinir sistemini düzenonsızlığı


Yöntem: Çalışmaya gelişmsel kekemeliğini olan 26 hasta ve yazı açıldıkta benzer, normal konuşması olan 17 sağlıklı kontrol alınmıştır. Olguların tümü erkek ve 19-25 yaş arasında olup. Kekemeler bir dil-konuşma tera- pisi uzmanı tarafından Kekemelik Südol Oğlucu ile derecelendirilmiştir. Olgu- larının tümüne Beck Depresyon ve Anksiyete Envanterleri uygulanmıştır. Otomon sinir sistemi 24-saatlik Holter monitozyorasyonu ile kalp atım değişikliği ol- çülecek değerlendirilmiştir. Zaman düzleminde yapılan kalp atım değişikliği analizlerinde, aralıkların 50 ms den fazla fark bulunduğuna dayandırır RR interval çatımların whipessi (pNN50 %), komşu RR intervalleri arasındaki farkın karelerinin ortalamasını (RMSSD, ms) ve bütün NN (normal-normal) aralıklarının ortalamalarını standart sapması (SDNN, ms) değerlendiril- di. Düşük frekans bölgelerinin gücünü (LF, 0.04-0.15 Hz), yüksek frekans bölgelerinin gücünü (HF, 0.15-0.40 Hz), LF/HF oranını, normalleştirilmiş bir- rımledeki LF ve HF güçleri ile bütün NN aralıklarının varyanını (total güç, ms2) değerlendirmek için freksan düzlemi analizler uygulandığı.


Anadır sözümlü: Kekemelik, otonom sinir sistemi, kalp hız değişikliği

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ABSTRACT: Autonomic nervous system imbalance in young adults with developmental stuttering

Objective: Autonomic nervous system plays a key role on motor speech and its regulation. On the other hand, physiological changes associated with activation of branches of autonomic nervous system in relation to emotions may also affect speech regulation. Thus, autonomic nervous system dysregulation may impair rate, rhythm, and general flow of speech or may exacerbate speech disfluency. However, the studies of autonomic reactions in persons with developmental stuttering are very limited. The purpose of the study is to evaluate whether autonomic nervous system dysregulation is responsible for persistent developmental stuttering in young adults.

Method: We studied 26 patients with persistent developmental stuttering and 17 normal speakers similar for age as healthy controls. The study comprised men who were between the ages of 19 and 25 years. Patients were examined by the speech pathologist using the Stuttering Severity Instrument (SSI-3). Beck Anxiety and Depression Inventories were performed to all subjects. Autonomic nervous system function was assessed by the 24-hour Holter monitoring for heart rate variability. Time-domain analyses were performed to evaluate the percentage of successive normal sinus RR intervals >50 ms (pNN50 %), the squares root of the mean of the sum the differences of squares between adjacent NN intervals (RMSSD, ms), and mean of the standard deviations of all NN (normal-normal) intervals of the entire recording (SDNN, ms). Frequency-domain analyses were performed to evaluate low-frequency power (LF, 0.04-0.15 Hz), high-frequency power (HF, 0.15-0.40 Hz), the ratio of LF to HF (LF/HF), HF and LF in normalized units, and variance of all NN intervals (total power ms2).

Results: In the stutterers, the mean onset of stuttering was 7.9±3.7 years (range: 3 - 17 years) and the mean duration of stuttering was 13.0±4.2 years (range: 2 - 20 years). Depression and anxiety scores were significantly higher in the stutterers than in those of the normal speakers. The stutterers had higher RMSDD and, lower LF, LF/HF and normalized LF values than the normal speakers. Subjective anxiety and total anxiety scores were negatively correlated with LF and total power.

Conclusions: Lower LF, the normalized LF and LF/HF suggest sympathetic imbalance in persons who stutter. Higher RMSDD in the stutterers may indicate a shift of sympathetic-vagal balance towards parasympathetic predominance. The results suggest that general autonomic nervous system imbalance might render the person prone to speech disfluencies. If these results are replicated in larger samples, they might provide some contribution in explaining the underlying pathophysiology of developmental stuttering.

Key words: Stuttering, autonomic nervous system, heart rate variability


INTRODUCTION

Stuttering is known to be a developmental disorder with impairment in speech fluency, which is characterized by frequent repetitions and prolongations of sounds or syllables. Persistent developmental stuttering affects 1% of adults, and it may impair social and occupational functioning (1). Research concerning the nature of stuttering has produced an extensive amount of data during the past century and many different explanatory models of stuttering causation have been proposed.
Traditionally, etiology has been defined in terms of predisposing, precipitating and perpetuating factors, but the mechanisms behind the speech disruptions and the speech initiation problems are yet unclear (2). With many experts agreeing on a strong neurological component, hypotheses about proximate causes of persistent developmental stuttering have focused on dysfunction of speech motor control, atypical lateralization of speech and language processes (3,4), deficiencies of the language production system (5,6), sensory impairments, in particular auditory (7), or a complex combination of motor and linguistic deficits (8). On the other hand, anxiety has been assigned various roles in theories of stuttering. Whereas, some view anxiety as the main cause of the disorder, others treat it as a mediating variable be it precipitating, perpetuating, or aggravating factors (9).

Autonomic nervous system (ANS) directly and/or indirectly plays a key role on motor speech and its regulation. The parasympathetic system is mainly passing through the two vagus nerves from the brain stem. The vagus nerves send autonomic fibers to not only the heart, lungs, and digestive organs, but also non-autonomic fibers to organs involved in speech, like the larynx, pharynx, and soft palate (10). On the other hand, the sympathetic system is often discussed in relation to emotions, such as stress and anxiety. Therefore, physiological changes associated with activation of the sympathetic branch of the ANS in relation to emotions may affect speech regulation (2). However, the studies of autonomic reactions in persons with stuttering are very limited. Two of the most meticulous studies of autonomic reactions in stutterers were made by Peters and Hulstijn, and Weber and Smith (11,12). Their studies investigated the measured skin conductance, pulse volume, and heart rate in persons with/without stuttering, before, during, and after speech task. Supporting each other, their results bring into mind that anticipation of a spontaneous speech task was associated with autonomic co-activation in the persons who stuttered. Caruso and colleagues also found that the mean heart rate of the persons with stuttering was significantly lower than that of the persons without stuttering, with increasing difference as the task became more stressful during the tasks (13).

The ANS activity is measured by a series of tests including cardiovascular autonomic function tests (heart rate variability, heart rate and blood pressure responses to the Valsalva maneuver and upright tilt test), pupillometry, skin conductance, sudomotor axon reflex test, and thermoregulatory sweat test (14). Heart rate variability (HRV) is a particularly sensitive method used to study autonomic dysfunction (15). It shows the extent of average heart rate fluctuations and reflects the interplay and balance between sympathetic and parasympathetic input displayed on the cardiac pacemaker (16).

ANS dysregulation can impair rate, rhythm, and general flow of speech or may exacerbate speech disfluency. However, possible relationship between developmental stuttering and autonomic nervous system imbalance seldom has been investigated. The purpose of this study is to show whether autonomic dysregulation is responsible for persistent developmental stuttering in young adults. Therefore, autonomic activity and sympatho-vagal balance were aimed to be evaluated by measuring HRV.

**MATERIALS AND METHODS**

**Subjects**

This was a cross-sectional case control study performed in collaboration with the departments of Psychiatry and Cardiology at the Hospital of Gulhane Military Medical Faculty between September 2007 and May 2008. We studied 26 patients with persistent development stuttering and 17 normal speakers similar for age as healthy controls. The study comprised men who were between the ages of 19 and 25 years (Table 2). Developmental stuttering was diagnosed according to DSM-IV criteria by a psychiatrist. After then a speech pathologist evaluated speech and stuttering severity.

All participants had normal bilateral hearing with simple hearing examination. Subjects with a history of convulsions, central nervous system infections, cerebrovascular diseases, cranial trauma, endocrine and metabolic diseases, or any chronic drug use and those who have mental retardation, learning disorders and severe psychiatric disorders were excluded from
this study. No subject in either group had autonomic symptoms such as fatigue, syncope, dizziness etc. and did not receive any drug (psychotrops, sympathomimetics, parasympatholytics etc.) before and during the study period. All participants were asked to refrain from heavy smoking, excessive eating or exercising during the study period.

All participants gave written consent to a protocol approved by the Ethics Committee of the Gulhane Military Medical Faculty.

Procedure

In first phase of the study, a psychiatrist initially conducted the Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) (17,18). After that, our semi-structured socio-demographic information form, the Beck Depression and the Beck Anxiety Inventory tools were performed to the subjects. In the second phase, all patients were evaluated by the speech pathologist using the Stuttering Severity Instrument for Children and Adults-Third Edition (SSI-3). In the third phase, all subjects were performed the twenty-four-hour Holter monitorization for heart rate variability measurement.

Measures

Beck Anxiety Inventory (BAI): This self-report scale consists of 21 items. Each item is rated between 0 (never) and 3 (all the time). Increasing scores indicate severity of the intensity of anxiety symptoms. Possible scores range between 0 and 63. It is composed of two parts, including subjective and somatic anxiety. The BAI was developed by Beck et al., and the validity and reliability study in Turkey was performed by Ulusoy and colleagues (19, 20).

Beck Depression Inventory (BDI): Symptoms and severity of depression were evaluated using the Turkish version (21) of the Beck Depression Inventory (BDI) (22). The BDI is a 21-item self-report questionnaire. The 21 items correspond to symptoms such as mood, pessimism, and suicidal ideas. Subjects rate each item on a 4-point likert scale from 0 (absent) to 3 (severe). The recommended cutoff 17 is used to define depression; higher scores indicate greater depression. The BDI is an internally consistent and valid measurement. The Cronbach alpha was 0.90 for the BDI (21).

The Stuttering Severity Instrument for Children and Adults-Third Edition (SSI-3): The SSI-3 was developed by Riley (23). This instrument measures the stuttering severity of both children and adults for clinical and research use. The SSI-3 Test Record and Frequency Computation Form is divided into four major areas: frequency (converted to scale scores 0 through 18); duration (converted to scale scores 0 through 18); physical concomitants (rated by degree of distractibility 0 through 20); and severity conversion tables for preschool children (ages 2-10 through 5-11), school-age children (ages 6-1 to 16-11), and adults (ages 17-0 and older). The levels of severity equivalents of SSI-3 total overall scores for adults are: 1) very mild (scores of 17 and below), 2) mild (scores between 18 and 24), 3) moderate (scores between 25 and 31), 4) severe (scores between 32 and 36), and 6) very severe (scores of 37 and higher) (23).

Twenty-four-hour Holter monitorization and heart rate variability measurements: The subjects were monitored for 24 hours with Delmar–Impresario, General Electric Holter system for assessment HRV (Irvine, CA, USA). RR is defined as the beat-to-beat interval between heart cycles on the basis of distances between R-peaks of the ECG. The morphology and rhythm characteristics of all QRS complexes should be classified to distinguish between cardiac cycles of sinus rhythm and other origin. Only RR intervals between the normal sinus rhythm beats (the so-called normal-to-normal or NN intervals) should be considered. Therefore, ectopic beats (coupling interval and compensatory pause) and arrhythmic events have to be excluded from further analysis (16). The resulting sequence of NN intervals can then be analyzed in many different ways that can be distinguished in standard measurements and nonlinear methods. We performed two main analyses for HRV: Time Domain and Frequency Domain Analyses (Table 1). Time-domain analyses were performed to evaluate the percentage of successive normal sinus RR intervals >50 ms (pNN50 %), the squares root of the mean of the sum the squares of differences between adjacent NN intervals (RMSSD; ms), and mean of the standard deviations of all NN (normal-normal) intervals of the
entire recording (SDNN; ms). Frequency-domain analyses were performed to evaluate low-frequency power (LF; 0.04-0.15 Hz), high-frequency power (HF; 0.15-0.40 Hz), the ratio of LF to HF (LF/HF), LF and HF in normalized units, and variance of all NN intervals (total power ms$^2$).

### Statistical Analysis

Differences between both groups were determined using the Mann Whitney-U test for continues variables according to the non-parametrical distribution of the data and analyzed with $\chi^2$ test variables for categorical variables. The correlations of data were tested by using the Spearman's correlation test. The SPSS (Statistical Package for Social Sciences) v.11.0 program was used in all analyses, and the level of significance was accepted as $p<0.05$.

### RESULTS

The mean age of the stutterers was $20.8 \pm 1.3$ years and that of the normal speakers was $21.6 \pm 2.0$ years with no significant difference between the groups ($p > 0.05$). The mean duration of stuttering was $13.0 \pm 4.2$ years (range: 2 - 20 years). The mean onset of stuttering was $7.9 \pm 3.7$ years (range: 3 - 17 years). Mean stuttering severity score was $3.7 \pm 1.3$ (range: 1 - 5). One of the subjects had very mild stuttering, 5 subjects exhibited mild stuttering, 5 subjects had moderate stuttering, and 5 subjects had severe stuttering. The remaining 10 subjects exhibited very severe stuttering.

In the stuttering group, 10 (38.5) subjects had DSM-IV psychiatric Axis I diagnoses, with anxiety disorder-not otherwise specified (n=7), adjustment disorder with anxiety (n=2), and social anxiety disorder.
The two groups were similar in terms of age, educational level, marital status and smoking (p>0.05). Depression and anxiety scores were significantly higher in the stutterers than in those of the normal speakers (p<0.01) (Table 2).

The stutterers had higher RMSDD values than the normal speakers (Z=1.99, p=0.047). The stutterers were found significantly lower values of LF, LF/HF and normalized LF than the normal speakers (Z=2.14, p=0.033, Z=2.36 p=0.018 and Z=3.53 p=0.000, respectively). However, there were not difference between groups for pNN50, SDNN, HF, normalized HF, total power and the global sympathetic index (GSI) (p>0.05) (Table 3).

We performed correlation analysis to show whether depression and anxiety levels associate with HRV parameters in the stuttering group. There was no correlation between depression scores and HRV parameters. LF and total power were merely negatively correlated with subjective anxiety scores (r=-0.49 p=0.011 and r=-0.41 p=0.039, respectively) and total anxiety scores (r=-0.44 p=0.023 and r=-0.41 p=0.037, respectively). There was no correlation between stuttering severity and HRV parameters as well as anxiety levels.

### DISCUSSION

Our study was aimed to investigate whether persons who stutter have the imbalance in the functionality of the ANS as determined by HRV, which is commonly used to evaluate parasympathetic tone and sympatho-vagal balance (16,27). We studied only young adult men as to control heterogeneity, such as sex and age. We found that the young adult men who stutter had significantly lower LF, normalized LF and LF/HF components, and higher RMSDD than the normal speakers. In addition, anxiety scores, particularly subjective anxiety were negatively correlated with LF and total power of HRV.

(n=1). The two groups were similar in terms of age, educational level, marital status and smoking (p>0.05).

### Table 2: Socio-demographic and clinic characteristics in the subjects who stutter and the normal speakers

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Stutterers (n=26)</th>
<th>Normal Speakers (n=17)</th>
<th>Statistics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)§</td>
<td>20.0 (19-23)</td>
<td>21.0 (19-25)</td>
<td>Z=1.67</td>
<td>.95</td>
</tr>
<tr>
<td>Educational level (year)¹</td>
<td>8.0 (5.0-15)</td>
<td>8.0 (5.0-13)</td>
<td>Z=0.55</td>
<td>.58</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>3 (11.5%)</td>
<td>2 (11.8%)</td>
<td>X²=0.001</td>
<td>.98</td>
</tr>
<tr>
<td>Single</td>
<td>23 (88.5%)</td>
<td>15 (88.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (61.5%)</td>
<td>6 (35.3%)</td>
<td>X²=3.83</td>
<td>.92</td>
</tr>
<tr>
<td>No</td>
<td>10 (38.5%)</td>
<td>11 (64.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beck Depression Inventory²</td>
<td>15.5 (3.0-39)</td>
<td>4.0 (0-7.0)</td>
<td>Z=4.44</td>
<td>0.0001**</td>
</tr>
<tr>
<td>Beck Anxiety Inventory²</td>
<td>15.0 (0-52)</td>
<td>5.0 (2.0-9.0)</td>
<td>Z=2.83</td>
<td>.005**</td>
</tr>
</tbody>
</table>

¹Data are showed as median (min-max)

**p<0.01

<table>
<thead>
<tr>
<th>HRV parameters</th>
<th>Stutterers (n=26)</th>
<th>Normal Speakers (n=17)</th>
<th>Z</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pNN50 (%)</td>
<td>29.53 (3.5-55)</td>
<td>20.60 (3.9-36)</td>
<td>1.64</td>
<td>.101</td>
</tr>
<tr>
<td>RMSDD (ms)</td>
<td>78.09 (26-215)</td>
<td>64.00 (26-96)</td>
<td>1.99</td>
<td>.047*</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>185 (48-238)</td>
<td>194.4 (120-263)</td>
<td>1.14</td>
<td>.253</td>
</tr>
<tr>
<td>LF (ms²)</td>
<td>260.40 (50-1450)</td>
<td>702.4 (223-1448)</td>
<td>2.14</td>
<td>.033*</td>
</tr>
<tr>
<td>HF (ms²)</td>
<td>280 (50-3440)</td>
<td>386.4 (32-3443)</td>
<td>.124</td>
<td>.901</td>
</tr>
<tr>
<td>Total power (ms²)</td>
<td>1010 (190-5700)</td>
<td>2074 (695-5709)</td>
<td>.870</td>
<td>.385</td>
</tr>
<tr>
<td>LF / HF</td>
<td>1.14 (0.33-2.60)</td>
<td>1.82 (0.33-15.09)</td>
<td>2.36</td>
<td>.018*</td>
</tr>
<tr>
<td>Normalized LF</td>
<td>38.33 (18.18-64 20)</td>
<td>60.33 (23.39-92 68)</td>
<td>3.53</td>
<td>.001**</td>
</tr>
<tr>
<td>Normalized HF</td>
<td>37.91 (14.58-70 78)</td>
<td>33.19 (6.14-70 78)</td>
<td>.669</td>
<td>.385</td>
</tr>
<tr>
<td>GSI</td>
<td>2.89 (0.57-7.10)</td>
<td>4.12 (0.58-20.68)</td>
<td>1.89</td>
<td>.059</td>
</tr>
</tbody>
</table>

¹Data are showed as median (min-max)

*p<0.05; **p<0.01; LF: Low Frequency; HF: High Frequency; GSI: Global Sympathetic Index; HRV: Heart Rate Variability
The RMSSD and pNN50 reflect mainly vagally mediated influences to the heart (16,28); likewise HF and especially normalized HF have been recognized to give insight into vagal activity (29,30). Although LF and normalized LF have sometimes been treated as an indicator of sympathetic activity (16), LF is considered as a better indicator of the joint effects of sympathetic and parasympathetic activity (16,28). Namely, LF band reflects both sympathetic and parasympathetic activity and is associated with baroreflex activity (31,32). The LF/HF ratio is also thought to reflect sympathetic/parasympathetic activity ratio or sympatho-vagal balance by some authors (31,33,34). In our study, lower LF, the normalized LF and LF/HF suggest sympatho-vagal imbalance in persons who stutter. In addition, higher RMSDD in the stutterers could indicate a shift of sympatho-vagal balance towards parasympathetic predominance.

Previous studies of ANS activity in stuttering have been to investigate whether stutterers experience greater autonomic arousal than normal speakers. The results of these studies usually indicate that during rest and non-speech conditions, autonomic activity in stutterers and normal speakers is similar. But, during the anticipation period before spontaneous speech and speech task, the stutterers show less increase of heart rate than normal speakers (11) or heart rate of stutterers reduces, whereas normal speakers show an increase of heart rate (12). The tendency for persons who stutter to show suppression of the heart rate during speech-related stress is supported by the results from a study by Caruso and colleagues (13). Depending on these results, Alm suggests that anticipation of a spontaneous speech task was associated with autonomic coactivation in the persons who stutter (2). Coactivation means that an increase of sympathetic activity is paralleled by an increase of parasympathetic activity. Bernston and colleagues suggest that in some situations the two branches of the ANS are coactivated. In this case a large increase in ANS activity will have a small effect on the heart rate, since the accelerating sympathetic effect is inhibited by the parasympathetic system (35). However, our results do not indicate an increased sympathetic activation together with parasympathetic activation in stuttering persons. Our results reflect a shift of sympatho-vagal balance towards parasympathetic predominance.

The relation between stuttering and emotional factors has long been a matter of debate. Many people who stutter have the experience that stuttering is influenced by their emotional reactions, and this is also a common clinical experience. Furthermore, anxiety has been assigned various roles in theories of stuttering (2). Empirical studies of anxiety and stuttering have mostly supported a positive relationship (36-38). In our study, anxiety scores were significantly higher in the stutterers than in those of the normal speakers. However, there have been studies that failed to find that people who stutter are significantly more anxious than normally fluent speakers (11, 39). In addition, many studies have been reported a positive relation between the severity of stuttering and level of anxiety (12,13,40). But, there were no correlations between stuttering severity and anxiety levels in our study. We found that LF and total power were negatively correlated with anxiety levels. Probably, in our study, lower values of LF in the stutterers may be related to anxiety levels.

As for the limitations in the present study, first, the design was cross-sectional and the sample size was not large enough. So, further large-scale clinical studies are needed. Second, HRV might be affected from age, gender, smoking status and Body Mass Index (41-43). Our study was executed in highly selected group of stuttering subjects as a narrow range age, only male gender and limited cigarette smoking. However, all the factors were not possible to get under control. Third, other tests for evaluation of ANS activity including pupillometry, skin conductance, sudomotor axon reflex test, and thermoregulatory sweat test should have been supported.

Previous studies of ANS activity in stuttering have measured short-term heart rate changes during resting, speech and non-speech tasks. To the best of our knowledge, our study is the first evaluating general ANS activity was evaluated by measuring long-term HRV (at 24-h recordings) in adult stutterers. Therefore, our result reflects general ANS activity rather than ANS activity during speech. In conclusion, the results were consistent with a shift of sympatho-vagal balance towards parasympathetic
Autonomic nervous system imbalance in young adults with developmental stuttering

We suggest that general ANS imbalance with parasympathetic predominance might render the person prone to speech disfluencies. If these results are replicated in larger samples, they might provide some contribution in explaining the underlying pathophysiology of stuttering and in developing rational approaches in treatment of stuttering.

References:


