Association Between 50 bp Insertion/Deletion Polymorphism in Promoter of the Superoxide Dismutase-1 and Temperament

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Abstract

Introduction: Temperament (mizaj) plays an important role in society's general health as well as in diagnosis and treatment of diseases. Despite its effectiveness, the mechanisms of temperament-dependent treatment in practical Iranian Traditional Medicine (ITM) has not been well understood yet. This study aimed to evaluate the association between the temperament and superoxide dismutase-1 (SOD1) polymorphism.

Methods: The study was carried out on healthy blood donors. All participants were from Fars province, southern Iran. To determine the participants' temperaments, a self-reported identification scale was used. Two hundred eighty males with any of 4 simple temperaments (Warm, Cold, Moist, and Dry) were included. The SOD1 genotypes were determined using a polymerase chain reaction (PCR)-based method. Multinomial logistic regression was used to calculate odds ratios (ORs) and 95% CI for the association of temperament with SOD1 polymorphism.

Results: No association was found between the insertion/deletion (Ins/Del) polymorphism of SOD1 and each of the temperament groups.

Conclusion: The results of this study indicated that the temperament is not affected by the Ins/Del polymorphism of SOD1 and each of the temperament groups.

Keywords: Temperament, Superoxide dismutase-1, Polymorphism
nucleus, peroxisomes, and mitochondria. It is a metalo-
enzyme which binds to copper and zinc and catalyzes
the conversion of toxic superoxide radicals to hydrogen
peroxide (H$_2$O$_2$) and molecular oxygen (O$_2$). The loss
of SOD1 activity, thus, could lead to the accumulation of
reactive oxygen species (ROS). ROS, which play an im-
portant role in many physiological functions, are regular-
ly produced in cells. However in excess, ROS may react
with fatty acids, proteins and DNA, thereby causing dam-
age or death to the cells.

Several genetic polymorphisms of SOD1 have been shown
to be associated with the risk of Alzheimer disease, liver and renal disease, cancer, and so on. There is a 50 bp in-
sertion/deletion (Ins/Del) polymorphism in the promoter region of this gene. The 50 bp-deleted region which binds
to multiple transcription factors has been shown to be as-
sociated with reduced promoter and enzymatic activity of
SOD1.

Previously, it was shown that the frequency of DNA dam-
age (nuclear buds) and cell death biomarkers (condensed chromatin, karyorrhexis, pyknotic changes, and karyolitic cells) significantly differ between certain temperament groups. Moreover, the association of polymorphisms in antioxidant enzymes of glutathione S-transferase M1 and T1 and warm temperament has been reported. These findings support the idea that the antioxidant system may affect the temperament modes. Therefore, the present study was carried out to evaluate the association of temperament with SOD1 50 bp Ins/Del polymorphism as a potential genetic candidate.

### Materials and Methods

The study was carried out on healthy individuals referred for blood donation to Shiraz Blood Transfusion Organization from November to December 2016. All participants were from Fars province, southern Iran, and aged between 20-40 years. To determine the participants’ temperaments, a self-reported identification scale constructed for healthy individuals was used. Two hundred eighty males with equilibrium or any of 4 simple temperaments (warm, cold, moist, and dry) were included in the study. The primers and polymerase chain reaction (PCR) conditions for determining the SOD1 genotypes were the same as those reported previously. Multinomial logistic regression was used to calculate odds ratios (ORs) and 95% CI for the association of temperament with SOD1 polymorphism.

### Results

As revealed by the data of the age, no significant differ-
ence was observed between the means of age in different
groups. The allele frequencies of SOD1 gene 50 bp variant
in each of the temperament groups is shown in Table 1. Because of low prevalence of the Del allele, Del/Del and Ins/Del genotypes were combined with each other as Del/- genotype for statistical comparisons. To control the possible effect of age, the association between SOD1 and temperament was examined using multinomial logistic regression while controlling for the age, and the equilibrium group was selected as the reference group. Neither the Ins/Ins nor the Del/- genotypes were associated with any of the simple groups (Table 2).

### Table 1. Allele Frequencies of SOD1 Gene 50 bp Variant in Each Temperament Group

<table>
<thead>
<tr>
<th>Temperament</th>
<th>Ins Frequency (%)</th>
<th>Del Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm</td>
<td>110 (92)</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Cold</td>
<td>61 (92)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Moist</td>
<td>122 (86)</td>
<td>20 (14)</td>
</tr>
<tr>
<td>Dry</td>
<td>102 (88)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>Equilibrium</td>
<td>102 (88)</td>
<td>14 (12)</td>
</tr>
</tbody>
</table>

### Table 2. Association Between Temperaments and SOD1 Polymorphism

<table>
<thead>
<tr>
<th>Temperament/Genotypes</th>
<th>N</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>P</th>
<th>Adjusted OR*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ins/Ins</td>
<td>51</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del/-</td>
<td>9</td>
<td>0.61</td>
<td>0.24-1.56</td>
<td>0.304</td>
<td>0.63</td>
<td>0.24-1.61</td>
<td>0.330</td>
</tr>
<tr>
<td>Cold</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ins/Ins</td>
<td>28</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del/-</td>
<td>5</td>
<td>0.62</td>
<td>0.20-1.92</td>
<td>0.406</td>
<td>0.63</td>
<td>0.20-1.96</td>
<td>0.426</td>
</tr>
<tr>
<td>Moist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ins/Ins</td>
<td>57</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del/-</td>
<td>14</td>
<td>0.85</td>
<td>0.36-1.99</td>
<td>0.708</td>
<td>0.89</td>
<td>0.38-2.11</td>
<td>0.792</td>
</tr>
<tr>
<td>Dry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ins/Ins</td>
<td>46</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del/-</td>
<td>12</td>
<td>0.90</td>
<td>0.37-2.19</td>
<td>0.821</td>
<td>0.89</td>
<td>0.37-2.17</td>
<td>0.801</td>
</tr>
</tbody>
</table>

*Adjusted for age.

Reference group: Equilibrium (Ins/Ins = 45, Del/- = 13).
Discussion
There are increasing evidence indicating the association of temperament with biological factors such as autonomic and immune systems, blood groups, enzymatic variation, and body composition. More interestingly, recent molecular biology studies have revealed that temperament modes are associated with distinct patterns of gene expressions as well as protein-protein interactions. The present results indicated that the temperament was not affected by the SOD1 Ins/Del polymorphism. This is the first study on the association of SOD1 polymorphism with temperament. The sample size which might not be large enough to reach a convincing conclusion is the limitation of the present study. Another limitation of this study which should be taken into consideration is the unavailability of general health status of participants. However, despite the fact that physicians ignore some diseases during screening, it should be noticed that usually most of volunteers verified for blood donation are in well physical and mental health.

Conclusion
In conclusion, this study did not support the association between SOD1 Ins/Del polymorphism and any of the temperament modes. However, Ins/Del polymorphism of SOD1 needs to be further analyzed in future studies to verify our observation. Performing larger studies with greater samples and with other SOD1 polymorphisms as well as other polymorphisms in genes of antioxidant system is recommended.

Ethical Approval
This study was approved by Ethics Committee of Shiraz University (ECBDE-SU-9-6177616), and each subject was informed about the objectives of the study.

Competing interests
Not declared.

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References