Side-to-side Asymmetry in Trigeminal Neuralgia
— Multiple Factors Theory —

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Abstract: The right side was affected in 61% of reported cases and the left side was affected in 39% of approximately 30,000 patients with trigeminal neuralgia (TN) affected on only one side. Side-to-side asymmetry of neurovascular compression in healthy persons cannot account for side-to-side asymmetry in TN. Size asymmetry and shape asymmetry of the rotundum and ovale foramen may account for the higher incidence of TN on the right side. This paper proposes a multiple factors theory: the summation of multiple factors reaches a critical level at which TN occurs. It is rational that entrapment of the maxillary and mandibular nerves when they cross the ovale and rotundum foramens is one of the factors which cause TN. The multiple factors theory can account for a TN patient without neurovascular compression and a healthy person with neurovascular compression.

Key words: trigeminal neuralgia, side-to-side asymmetry, multiple factors theory, the rotundum and ovale foramen, etiology

Introduction
Trigeminal neuralgia (TN) causes sudden, usually unilateral, severe brief stabbing recurrent pains in the distribution of one or more branches of the trigeminal nerve. Pain is reported to be more lateralized on the right. This paper reviews the side-to-side asymmetry of TN.

Side-to-side asymmetry in trigeminal neuralgia
To analyze TN, many articles were collected at random. Based on the collected articles, the right side was affected in 61% of reported cases and the left side was affected in 39% of approximately 30,000 patients affected on only one side (Table 1).

Side-to-side asymmetry of neurovascular compression in healthy persons
Elongation of an artery at the point where the trigeminal nerve root is located was found on the left side in 31, on the right side in 28, and on both sides in 10 of the 159 non-TN patients in a conventional biplane vertebral angiography study. Two studies with cadavers (20 cadavers and 65 cadavers) found that neurovascular contact or compression on the left side was more common than that on the right side, although there was no significant difference. Adamczyk et al. reported that contact between TN and an artery was found in 30 nerves (25%, 17 on the right, 13 on the left) out of 120 nerves (60 patients) in an MRI study (angio-3D-TOF images). The blood vessel was parallel to the nerve root in 14 nerves (11.7%) and crossed it perpendicularly or at an acute angle in 15 nerves (12.5%). Side-to-side asymmetry of neurovascular compression in healthy persons cannot account for side-to-side asymmetry in TN.

Cause of side-to-side asymmetry in TN
Gardner et al. reported that the apex of the right petrous bone was higher than the left in 46%, and the left was higher than the right in
34%, and they were of equal height in 20% in 115 patients with unilateral TN. These figures are similar to those for 200 controls (non-TN patients) (right side was higher in 47.5%, left side was higher in 29%, equal in 23.5%). However, the neuralgia was on the side of the higher petrous apex in 60% of cases, and on the side of the lower petrous apex in only 20% (with the height of both sides at the same level in 20%). The average height of the apex of the petrous bone in women with TN rose from the fourth to the eighth decade. They thought the upward progression of the apex of the petrous bone was due to postmenopausal osteoporosis. Bjerrum et al. assessed the basilar impression from the level of the odontoid process in relation to McGregor’s line. It was found that the trigeminal impression at the apex of the petrous bone showed an unmistakable tendency to lie at a higher level on the affected side in 55 patients with TN. However, the slight tendency for a higher level of the trigeminal impression on the right side was not statistically significant in 100 controls (non-TN patients). Rothman et al. reported no association between the side of facial pain and an elevated ipsilateral petrous apex in 46 patients with TN and concluded that even if an elevated petrous ridge is a risk factor in TN, it must be a weak one.

Anatomical and radiological studies have shown that the rotundum and ovale foramen was a primary cause of TN and accounted for the higher incidence of TN on the right side. Ray et al. examined 35 dried human skulls and reported as follows: Mean length and width of foramen ovale were 7.46 mm and 3.21 mm on the right side and 7.01 mm and 3.29 mm on the left side, respectively. The shape of foramen ovale was typically oval in 43 (22 on the right, 21 on the left), almond shape in 24 (11 right, 13 left), round in 2 (1 right, 1 left), and slit-like in 1 (1 right). Yanagi examined approximately 230 dried human skulls (of age 10 or over) and found that the average diameter of the foramen rotundum and foramen ovale was 3.51 mm and 5.82 mm on the right side and 3.58 mm and 5.93 mm on the left side, respectively. Shape asymmetry as well as size asymmetry may account for the higher incidence of TN on the right side.

### Multiple factors theory

The peripheral cause of TN, central cause of TN, and peripheral origin central pathogenesis theory cannot account for side-to-side asymmetry in TN. However, no single theory can account for a TN patient without neurovascular compression, a healthy person with neurovascular compression, and side-to-side asymmetry in TN. I propose a multiple factors theory: the summation of multiple factors reaches a critical level at which TN occurs. Tumor or multiple sclerosis alone may be sufficient to cause TN (Fig. 1A) If a combination of neurovascular compression and other factors reaches the critical level, TN occurs (Fig. 1B). If a combination of other factors reaches the critical level, TN occurs (Fig. 1C). If a combination of neurovascular compression and other factors does not reach the critical level, TN does not occur (Fig. 1D). It is rational that entrapment of the maxillary and mandibular nerves when they cross the ovale and rotundum foramen is one of the factors which cause TN. Therefore, pain is reported to be more lateralized on the right. The multiple factors theory can account for a TN patient without

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**Table 1** Side-to-side asymmetry in trigeminal neuralgia

<table>
<thead>
<tr>
<th>Side</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Right</td>
<td>18,719 (61.0%)</td>
</tr>
<tr>
<td>Left</td>
<td>11,978 (39.0%)</td>
</tr>
</tbody>
</table>

This is the sum of the following articles. These articles were collected at random to analyze trigeminal neuralgia. To avoid overlap, articles of Jannetta et al. and an article of Zakrzewsk were removed from the review of Hamlyn and an article of Harris and an article of Peet et al. were removed from the review of White et al.
neurovascular compression, a healthy person with neurovascular compression, and side-to-side asymmetry in TN. The term “multiple factors” includes many factors such as tumor, multiple sclerosis, neurovascular compression, diabetes, unknown factors, and entrapment of the maxillary and mandibular nerves when they cross the ovale and rotundum foramens.

**Conclusion**

In conclusion, the right side was affected in 61% of reported cases and the left side was affected in 39% of approximately 30,000 patients affected on only one side. Side-to-side asymmetry of neurovascular compression in healthy persons cannot account for side-to-side asymmetry in TN. Size asymmetry and shape asymmetry of the rotundum and ovale foramens may account for the higher incidence of TN on the right side. I propose a multiple factors theory: the summation of multiple factors reaches a critical level at which TN occurs. It is rational that entrapment of the maxillary and mandibular nerves when they cross the ovale and rotundum foramens is one of the factors which cause TN.

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