益 2025年9月28日(日) 14:50 ~ 16:20 **金** Session Room 7 (Conference Room C)

[Symposium 106] Oral Splint Therapy for Tourette Syndrome: Bridging Dentistry and Psychiatry

Moderator: Yuki Oda (Hiroshima Oral Health Center)

[SY-106]

Oral Splint Therapy for Tourette Syndrome: Bridging Dentistry and Psychiatry

Jumpei Murakami¹, Kyoko Hoshino², Yoshihisa Tachibana³, Max A Tischfield⁴ (1. Osaka University (Japan), 2. Segawa Memorial Neurological Clinic for Children (Japan), 3. Kobe University (Japan), 4. Rutgers University (United States of America))

[SY-106-01]

Oral splint ameliorates tic symptoms in patients with Tourette syndrome

*Jumpei Murakami¹ (1. Osaka University Dental Hospital (Japan))

[SY-106-02]

Oral splint therapy for Tourette syndrome in Segawa Memorial Neurological Clinic for Children

*Kyoko Hoshino¹, Kazunori Takamori² (1. Segawa Memorial Neurological Clinic for Children (Japan), 2. Department of Pediatric Dentistry Nihon University School of Dentistryol of Dentistry. (Japan))

[SY-106-03]

Therapeutic Effects and Underlying Mechanisms of Oral Splint Use for Ameliorating Tic Symptoms in Tourette Syndrome

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[SY-106-04]

Modeling Genetic Heterogeneity in Tourette Syndrome: Dissecting Circuit and Behavioral Phenotypes in Mouse Models with High-Confidence Risk Mutations

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[SY-106] Oral Splint Therapy for Tourette Syndrome: Bridging Dentistry and Psychiatry

Jumpei Murakami¹, Kyoko Hoshino², Yoshihisa Tachibana³, Max A Tischfield⁴ (1. Osaka University (Japan), 2. Segawa Memorial Neurological Clinic for Children (Japan), 3. Kobe University (Japan), 4. Rutgers University (United States of America))

キーワード: Tourette Syndrome、Tic、Oral Splint

Tourette syndrome (TS) is a complex neuropsychiatric disorder characterized by repetitive, involuntary movements and vocalizations known as tics. Although pharmacological and behavioral therapies are commonly used, their effectiveness varies among individuals, and side effects can be burdensome. Recently, oral splint therapy has emerged as a promising intervention, showing potential in reducing tic symptoms. Despite this growing interest, the underlying mechanisms of its therapeutic effects remain unclear. This symposium aims to explore the potential and challenges of oral splint therapy for Tourette syndrome from a multidisciplinary perspective. By bringing together experts from dentistry, neurology, and neuroscience, we will discuss the clinical efficacy of dental splint therapy, its neurological implications, and possible underlying mechanisms. Through this interdisciplinary dialogue, we aim to deepen the understanding of oral splint therapy's role in managing TS and encourage further research and collaboration. Through this symposium, we will examine the clinical and scientific foundations of oral splint therapy for Tourette syndrome. The presentations will include a comprehensive review of clinical outcomes, neurological insights into tic modulation, and hypotheses on the neural mechanisms involved. By fostering collaboration between clinicians and researchers, we hope to inspire innovative therapeutic strategies and pave the way for evidence-based integration of oral splint therapy into TS management.

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Moderator: Yuki Oda (Hiroshima Oral Health Center)

[SY-106-01] Oral splint ameliorates tic symptoms in patients with Tourette syndrome

*Jumpei Murakami¹ (1. Osaka University Dental Hospital (Japan)) キーワード:Tourette syndrome、Oral Splint、Dentistry

Tourette syndrome (TS) is a neurodevelopmental and psychiatric disorder characterized by persistent motor and phonic tics, often accompanied by premonitory urges and psychiatric comorbidities. In this study, we investigated the potential therapeutic effects of a custom-made oral splint—commonly used in dental practice for temporomandibular disorders—on tic symptoms in TS patients. A total of 22 individuals with TS were assessed using the Tic Symptom Self-Report. Following oral splint application, mean motor and phonic tic scores significantly decreased from 15.3 to 11.0 and from 15.1 to 8.2, respectively—representing average reduction rates of 30% and 43%. These improvements were observed immediately and were sustained for over 100 days in many cases. Notably, 72.7% of patients showed dual improvements in both motor and phonic tics. Younger age at tic onset and at first hospital visit were significantly associated with longterm treatment efficacy. The splint may serve as a "sensory trick" by modulating proprioceptive input from jaw-closing muscles, potentially influencing insular cortex activity, which is known to be hyperactive in TS. These findings suggest that oral splints could offer a simple, non-pharmacological therapeutic option for managing TS-related tics, particularly in younger patients. Further research is warranted to validate these outcomes and elucidate the neurophysiological mechanisms involved.

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[Symposium 106] Oral Splint Therapy for Tourette Syndrome: Bridging Dentistry and Psychiatry

Moderator: Yuki Oda (Hiroshima Oral Health Center)

[SY-106-02] Oral splint therapy for Tourette syndrome in Segawa Memorial Neurological Clinic for Children

*Kyoko Hoshino¹, Kazunori Takamori² (1. Segawa Memorial Neurological Clinic for Children (Japan), 2. Department of Pediatric Dentistry Nihon University School of Dentistryol of Dentistry. (Japan))

キーワード:Tourette syndrome、oral splint therapy、phonic tic、YGTSS-J、PUTS

Background: Oral splint therapy for Tourette Syndrome (TS) is considered a breaking treatment because of no internal side effects like medications. We have begun research of with Osaka University Dental Hospital and Nihon University School of Dentistry. This study was approved by ethic committee of clinic (SMNCC20-03R2). Subjects: Five cases of TS were participated and two cases were ineligible due to dental caries. Clinical course, Yale Global Tic Severity Scale-Japan (YGTSSJ), Premonitory Urges for Tic Disorders Scale (PUTS), obsessive-compulsive and anxiety scale were also evaluated. Inclusion criteria: 1) patients who could visit regularly. 2) with severe phonic tics. 3) over 14 year-old. ④without dental caries. Informed consent was obtained. Results: Patients were 18F, 14F, 15F (second tried), 21F, 19M. YGTSSJ: Pre. Motor (M) $12.4 \pm 5.2 (19-5)$, Phonic (p) $12.0 \pm 100 (10-5)$ 3.8 (18–5), Impairment (I) 26 ± 7.3 (40–20), Total (T) 50.4 ± 11.2 (67–36). Post 1 mo. M 12.2 ± 4.2 (18-5), P 10.8 ± 3.3 (18-8), I 20.0 ± 8.9 (30-10), T 39.0 ± 16.3 (66-19) . Post 2 mo. M 11.6±2.4 (16-9) P 10.0±2.3 (16-9) I 17.5±7.4 (30-10) T 39.3±8.5 (53-29). PUTS: Pre 19.4±5.7 (27-12). Post 1 mo.17.3 ± 6.0 (27-11). Post 2 mo.22.3 ± 5.7 (27-13). Although with minimum change in scores, 4 reported high satisfaction at 1 month after. However, satisfaction decreased in 2 months. Anxiety improved mildly in one case. During this study, 8 cases were referred to the dentist with conditions such as glossitis, stomatitis, and bruxism, not for oral splint. Discussion: Oral splint therapy is still in verification, although the number was small and temporary research, it expressed somewhat effective. TS patients who resistant to medication and behavioral intervention might be applied oral splint therapy for short-term relief.

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[SY-106-03] Therapeutic Effects and Underlying Mechanisms of Oral Splint Use for Ameliorating Tic Symptoms in Tourette Syndrome

*Yoshihisa Tachibana¹ (1. Department of Physiology and Cell Biology, Kobe University Graduate School of Medicine (Japan))

キーワード: basal ganglia、insula、striatum、intralaminar thalamic nuclei、tic

Tourette syndrome (TS) is a neurodevelopmental disorder characterized by motor and vocal tics. TS is often accompanied by cognitive and emotional dysfunctions, including obsessive-compulsive disorder and attention-deficit/hyperactivity disorder. We previously reported that a removable oral splint ameliorates both motor and vocal tics in TS patients. However, the mechanism by which the oral splint exerts these effects remains unclear. To address this issue, we first examined the ascending pathways of the masticatory muscle spindles, which are activated by the insertion of the oral splint. We identified that proprioceptive information originating from these spindles is ultimately transmitted to the insular cortex via the supratrigeminal nucleus and the caudo-ventromedial region of the ventral posteromedial thalamic nucleus. We then investigated why modulation of orofacial proprioceptive input to the insula alleviates tic symptoms. Previous imaging studies have reported abnormal activity in the striatum and insula in TS patients. Given that dysfunction of the cortico-basal ganglia-thalamocortical circuits has been implicated in TS, we hypothesized that this network plays a critical role in symptom generation. To test this, we developed a drug-induced mouse model of tics by unilaterally injecting bicuculline, a GABA receptor antagonist, into the striatal motor region. In these mice, c-Fos immunoreactivity revealed neuronal activation in limbic structures (insular cortex, cingulate cortex, and amygdala) as well as in motor regions (M1, globus pallidus, and subthalamic nucleus) but also. Using anterograde and retrograde viral tracers, we mapped the anatomical route from basal ganglia output structures to limbic cortices and identified the intralaminar thalamic nuclei as key hubs linking these regions. Finally, we demonstrated that chemogenetic inhibition of the insular cortex or its thalamocortical input significantly reduced tic-like behaviors in the mouse model. These findings suggest that aberrant neuronal processing within both motor and limbic domains of the corticobasal ganglia-thalamocortical circuits contributes to tic generation in TS.

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[SY-106-04] Modeling Genetic Heterogeneity in Tourette Syndrome: Dissecting Circuit and Behavioral Phenotypes in Mouse Models with High-Confidence Risk Mutations

*Max Tischfield^{1,2} (1. Rutgers University, Department of Cell Biology and Neuroscience (United States of America), 2. Child Health Institute of New Jersey, Robert Wood Johnson Medical School (United States of America))

キーワード:Tourette Syndrome、Human Genetics、Animal Models、Behavioral phenotypes、Dopamine signaling

Tourette syndrome (TS) is a complex neurodevelopmental disorder characterized by motor and vocal tics, but its clinical manifestations extend far beyond these core symptoms. Many individuals with TS exhibit varying degrees of impulse control deficits, compulsive behaviors, and comorbid neuropsychiatric conditions such as autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), and obsessivecompulsive disorder (OCD). This phenotypic heterogeneity underscores that TS exists on a spectrum, shaped by diverse genetic and neurobiological contributors. However, this complexity presents a major challenge for translational research, particularly in developing animal models that accurately recapitulate human pathophysiology. In this talk, I will present recent findings from two novel transgenic mouse lines that harbor de novo human mutations in high-confidence TS risk genes: Celsr3, the most strongly associated gene with TS identified to date, and Ank3, identified in probands with TS, OCD, and autistic features. These models display both overlapping and distinct behavioral phenotypes, including deficits in sensorimotor gating, enhanced habitual responding, and possible effects on neuromuscular control and proprioception. Notably, these models exhibit repetitive motor behaviors, but they do not fully resemble human tics. Using behavioral assays, neural recordings, and circuit-specific manipulations, we dissect how these mutations affect dopamine signaling and corticostriatal function. Our findings underscore the importance of using multiple, genetically validated models to capture the spectrum nature of TS. By examining how different mutations may perturb distinct and overlapping neural circuits, we begin to map how genetic variability gives rise to phenotypic diversity. These insights offer a framework for understanding the mechanistic basis of TS and lay the groundwork for developing targeted interventions that may include modulation of proprioceptive pathways.