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分担研究報告書

糖尿病家族歴がある群の糖代謝と睡眠呼吸障害の関連：長浜コホートでの成績

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研究要旨

研究の目的：糖尿病家族歴（FHD）は 2 型糖尿病の危険因子である。睡眠呼吸障害（SDB）が FHD を有する患者における糖尿病発症に関連するか検討した。

方法： 7,477 人の一般住人検診参加者（ながはまコホート）に対して、加速度計と睡眠日誌で客観的睡眠時間を測定し SDB 重症度を評価した。糖尿病は HbA1c≥6.5・糖尿病への投薬で判定し、糖尿病の有病率、インスリン抵抗性、SDB 評価以前の約 5 年間に新規発症した糖尿病の有病率を評価した。

結果：1,569 人が FHD を有し、中等度から重度の SDB（MS-SDB）のある患者において、SDB のない参加者よりも糖尿病有病率は有意に高かった。多変量解析において、MS-SDB が FHD を有する女性でのみ糖尿病有病率と関連していた。FHD を有する参加者の中で、最近 5 年で発症した糖尿病有病率は、女性においてのみ MS-SDB と関連していた。

結論：MS-SDB は FHD を有する女性の糖尿病リスクと関連していた。FHD を有する女性の SDB の治療介入が糖尿病発症を予防するか検討が必要と考えられた。

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A. 研究目的

糖尿病家族歴(FHD)は 2 型糖尿病発症のリスクファクターであることは明らかであるが、睡眠呼吸障害(SDB)が糖尿病家族歴のある群の 2 型糖尿病発症に関連しているかが明らかでないので、その関連を明らかにすることを研究目的とした。

B. 研究方法

「ながはまコホート」7,477 名の参加者に対して、加速度計と睡眠日誌で客観的睡眠時間を測定し、その客観的睡眠時間と酸素飽和度計を用いて SDB の重症度を評価し、FHD、SDB、糖代謝異常(糖尿病の有病率、インスリン抵抗性、SDB 評価以前の約 5 年間に新規発症した糖尿病の有病率)の関連を横断的に検討した。

C. 研究結果

FHD を有する女性において、中等から重症の SDB は 2 型糖尿病の有病率の増加及びインスリン抵抗性の増大と有意な関連があり、近 5 年間に新規発症した糖尿病の有病率は中等症以上の SDB で 21.4%と高値であった(SDB 無し：1.1%, P <0.001)。また、糖尿病の有病率とインスリン抵抗性に対して、SDB と FHD は有意な交互作用が認められた。一方、FHD を有する男性において SDB と糖代謝異常の関連は認められなかった。

D. 考察

本研究は横断的であるが、糖尿病家族歴のある女性に中等以上の SDB が合併すると現状の２型糖尿病の頻度と過去５年間の２型糖尿病の発症が増えることを示し、その病態生理に性差が存在することを明らかにした。

E. 結論

中等症以上の SDB は FHD のある群の２型糖尿病の頻度に関連していた。FHD のある女性の SDB に対する治療が２型糖尿病の発症を予防するかは今後の検討すべき課題である。

F. 研究発表

1．論文

Minami T, Matsumoto T, Tabara Y, Gozal D, Smith D, Murase K, Tanizawa K, Takahashi N, Nakatsuka Y, Hamada S, Handa T, Takeyama H, Oga T, Nakamoto I, Wakamura T, Komenami N, Setoh K, Tsutsumi T, Kawaguchi T, Kamatani Y, Takahashi Y, Morita S, Nakayama T, Hirai T, Matsuda F, Chin K; Nagahama Study Group. Impact of sleep-disordered breathing on glucose metabolism among individuals with a family history of diabetes: the Nagahama study. J Clin Sleep Med. 2021 Feb 1;17(2):129-140. doi: 10.5664/jcsm.8796.

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SCIENTIFIC INVESTIGATIONS

Impact of sleep-disordered breathing on glucose metabolism among individuals with a family history of diabetes: the Nagahama study

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Study Objectives: It is well known that a family history of diabetes (FHD) is a definitive risk factor for type 2 diabetes. It has not been known whether sleep-disordered breathing (SDB) increases the prevalence of diabetes in those with an FHD.

Methods: We assessed SDB severity in 7,477 study participants by oximetry corrected by objective sleep duration determined by wrist actigraphy. Glycated hemoglobin ≥6.5% and/or current medication for diabetes indicated the presence of diabetes. In addition to the overall prevalence, the prevalence of recent-onset diabetes during the nearly 5 years before the SDB measurements were made was investigated.

Results: Of the 7,477 participants (mean age: 57.9; range: 34.2–80.7; SD: 12.1 years; 67.7% females), 1,569 had an FHD. The prevalence of diabetes in FHD participants with moderate-to-severe SDB (MS-SDB) was higher than in those without SDB (MS-SDB vs without SDB: all, 29.3% vs 3.3% [$P < .001$]; females, 32.6% vs 1.9% [$P < .001$]; males, 26.2% vs 11.7% [$P = .037$]). However, multivariate analysis showed that MS-SDB was significantly associated with a higher prevalence of diabetes only in FHD-positive females (odds ratio [95% confidence interval]: females, 7.43 [3.16–17.45]; males, 0.92 [0.37–2.31]). Among the FHD-positive participants, the prevalence of recent-onset diabetes was higher in those with MS-SDB than those without SDB, but only in females (MS-SDB vs without SDB: 21.4% vs 1.1%; $P < 0.001$).

Conclusions: MS-SDB was associated with diabetes risk in females with an FHD, and future studies are needed on whether treatment of SDB in females with an FHD would prevent the onset of diabetes.

Keywords: heritability, gene, environment, obstructive sleep apnea, effect modification

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BRIEF SUMMARY

Current Knowledge/Study Rationale: A family history of diabetes is a strong risk factor for type 2 diabetes. Although it is said that sleep-disordered breathing is also a risk factor for diabetes, whether there is an additional increase in the prevalence of diabetes in individuals with a family history of diabetes is not known.

Study Impact: In our large community-based study, moderate-to-severe sleep-disordered breathing was significantly associated with an increased prevalence of type 2 diabetes and of recent-onset type 2 diabetes during a period of nearly 5 years, especially in females with a family history of diabetes. Thus, moderate-to-severe sleep-disordered breathing might be associated with an increased prevalence of type 2 diabetes in females with a family history of diabetes.

INTRODUCTION

Sleep-disordered breathing (SDB), especially obstructive sleep apnea (OSA), is a common condition characterized by recurrent intermittent hypoxia during sleep and sleep fragmentation. Individuals with SDB have a high prevalence of comorbidities such as cardiometabolic disorders, particularly with concurrent obesity.[1,2] Of the comorbidities associated with SDB, abnormal glucose metabolism has been identified in both public health and clinical settings. Indeed, several studies have shown that the prevalence of moderate-to-severe OSA exceeds 30% in patients with diabetes worldwide.[3–5] Furthermore,