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Title: The effects and mechanisms of chronic intermittent hypoxia on insulin resistance and glucose tolerance in non-obese rats

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Body: Rationale: In this study, we aimed to determine whether CIH could affect insulin resistance and glucose tolerance, and investigated the potential mechanisms underlying these effects. Methods: We utilized an established rodent model of CIH. Briefly, the rats exposed to CIH were placed into a chamber from 8 am to 5 pm, five days per week, for five consecutive weeks, which the oxygen concentration in the chamber was adjusted between 7% and 21%, with each period lasting one minute (Nitrogen was introduced at a rate sufficient to achieve a FIO₂ of 7% within 30 s and to maintain this level for 10 s, then oxygen was introduced at a rate to achieve a FIO₂ of 21% within 20 s). Results: The results from intraperitoneal glucose tolerance tests (IPGTTs) indicated that glucose tolerance in non-obese rats was decreased in the CIH group compared with controls following 5 weeks of intermittent hypoxia. In the CIH group, the insulin resistance index increased sharply, while the resistin and leptin levels increased by 64% and 70%, respectively. However, the serum levels of adiponectin decreased by 40%. Moreover, the expression of hypoxia inducible factor-1 α (HIF-1 α) was significantly higher in CIH rats compared with controls, which suggested the presence of adipose tissue hypoxia. Conclusions: These results showed that CIH leads to insulin resistance and impaired glucose tolerance in a non-obese rodent model of OSAHS. Furthermore, these results suggest that these effects may result from the dysregulation of adiponectin, resistin and leptin, which might be caused by adipose tissue hypoxia.