drive and protect against target organ damage and metabolic derangement.

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Insulin-sensitive overweight/obese individuals remain as insulin sensitive and normotensive as lean subjects over 6 years

Alice Tang [1,2,3,*], Katherine T. Tonks [1,2,3], Leonie K. Heilbronn [4], Nicholas A. Pocock [1,3,5,6], Lesley V. Campbell [1,2,3], David E. James [7], Donald J. Chisholm [1,2,3], Jerry R. Greenfield [1,2,3,8], Dorit Samocha-Bonet [1,3,8]

[1] The University of New South Wales, Kensington, NSW, Australia
[2] Endocrinology, St Vincent's Hospital, Darlinghurst, NSW, Australia
[3] Garvan Institute of Medical Research, Darlinghurst, NSW, Australia
[4] The University of Adelaide, Adelaide, SA, Australia
[5] Bone Densitometry, St Vincent's Clinic, Darlinghurst, NSW, Australia
[6] Nuclear Medicine, St Vincent's Hospital, Darlinghurst, NSW, Australia
[7] Charles Perkins Centre, The University of Sydney, Camperdown, NSW, Australia

Background: While obesity is a strong risk-factor for insulin-resistance, some obese individuals are as insulin-sensitive as lean individuals. However, whether insulin-sensitive obesity is an enduring phenotype remains unknown.

Methods: Subjects were studied at the Garvan [1,2] (2007—2010) using hyperinsulinaemic—euglycaemic clamps and DXA to measure insulin resistance and body composition, respectively ($n = 101$, 'baseline studies'). Participants were categorised as lean (BMI < 25 kg/m^2), overweight/obese insulin-sensitive or overweight/obese insulin-resistant (Ob$_{sen}$ or Ob$_{res}$; above or below median glucose infusion rate, respectively). Subjects were followed up after 6 ± 1yr. Fifty-nine individuals had their weight, systolic (SBP) and diastolic blood pressure (DBP) measured; a sub-cohort agreed to participate in repeat clamp and DXA studies ($n = 42$).

Results: Average age at follow-up was 60 ± 11yr. Insulin sensitivity ($P = 0.43$), BMI ($P = 0.53$) and body fat mass ($P = 0.10$) did not change significantly over time in this cohort. Despite this, visceral abdominal fat ($P = 0.004$), SBP ($P = 0.002$) and DBP ($P < 0.001$) increased, without a difference between groups ($P_{interaction} \geq 0.34$). At baseline, insulin sensitivity was $90 \pm 40\%$ and $40 \pm 10\%$, relative to lean, in Ob$_{sen}$ ($P = 0.62$) and Ob$_{res}$ ($P < 0.001$), respectively. This finding persisted at follow-up ($78 \pm 31\%$, $P = 0.46$; and $44 \pm 15\%$, $P < 0.001$, in Ob$_{sen}$ and Ob$_{res}$ relative to lean, respectively). At baseline, SBP (120 ± 10 mmHg) and DBP (76 ± 7 mmHg) measured in Ob$_{sen}$ were not statistically different to lean (114 ± 14 mmHg, $P = 0.09$; and 71 ± 9 mmHg, $P = 0.051$, respectively), but were markedly lower than Ob$_{res}$ (136 ± 19 mmHg, $P = 0.01$; and 86 ± 9 mmHg, $P < 0.001$, respectively). This pattern also persisted at follow-up where Ob$_{sen}$ had similar SBP (126 ± 19 mmHg) and DBP (79 ± 10 mmHg) to lean (124 ± 21 mmHg, $P = 0.97$; and 79 ± 14 mmHg, $P = 0.99$, respectively), but values were lower than Ob$_{res}$ (143 ± 17 mmHg, $P = 0.02$; and 91 ± 12 mmHg, $P = 0.01$, respectively).

Conclusion: We observed that in Ob$_{sen}$, relative normotension and insulin sensitivity was preserved over 6 years, suggesting a phenotype distinct from Ob$_{res}$. These findings may partly explain relative protection from cardiovascular disease observed in Ob$_{sen}$ relative to Ob$_{res}$ in longitudinal studies.

References

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[8] Equal contributors.