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SHORT COMMUNICATION

A reduction in both visceral and subcutaneous fats contributes to increased adiponectin by lifestyle intervention in the Diabetes Prevention Program

Chao Zhang · Hao Luo · Feng Gao · Chun-Ting Zhang · Ren Zhang

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Abstract
Aims Adiponectin, an insulin-sensitizing adipokine, confers protection against type 2 diabetes. Although adiponectin is secreted exclusively from fat, contributions of visceral adipose tissue (VAT) versus subcutaneous adipose tissue (SAT) to adiponectin levels have not been fully understood. We aimed to examine correlations between changes in VAT and SAT volumes and changes in adiponectin levels.
Methods Here, we have investigated the correlations between ΔVAT and ΔSAT with Δadiponectin in participants of the Diabetes Prevention Program, a clinical trial investigating the effects of lifestyle changes and metformin versus placebo on the rate of developing type 2 diabetes. Data on VAT and SAT volumes, measured by computed tomography, and on adiponectin levels at both baseline and 1-year follow-up were available in 321 men and 626 women.
Results In men, Δadiponectin was highly significantly correlated with both ΔSAT ($r_s = -0.329$) and ΔVAT ($r_s = -0.413$). Likewise, in women, Δadiponectin was correlated with both ΔSAT ($r_s = -0.294$) and ΔVAT ($r_s = -0.348$). In the lifestyle arm, Δadiponectin remained highly significantly correlated with ΔSAT and ΔVAT in men ($r_s = -0.399$ and $r_s = -0.460$, respectively), and in women ($r_s = -0.372$ and $r_s = -0.396$, respectively), with $P < 0.001$ for all above correlations.
Conclusions We conclude that for both men and women, adiponectin changes are highly significantly correlated with changes in both SAT and VAT and that exercise- and weight-loss-induced reduction in both SAT and VAT contributes to the increased adiponectin.

Keywords Adiponectin · Subcutaneous adipose tissue · Visceral adipose tissue

Insulin resistance is a key feature of metabolic syndrome, which has dramatically increased in prevalence, mainly because of the global obesity epidemic. A reduced concentration of adiponectin, an insulin-sensitizing adipokine [1], precedes the onset of type 2 diabetes; conversely, increased adiponectin confers protection against type 2 diabetes [2, 3].

Increased visceral adipose tissue (VAT) is considered more strongly associated with type 2 diabetes than subcutaneous adipose tissue (SAT). Current evidence on the association between adiponectin and VAT versus SAT has not been conclusive. Importantly, to investigate the contributions of VAT versus SAT to adiponectin levels, it is necessary to examine the correlation between *changes* in adiponectin concentration and *changes* in VAT and SAT. However, such kind of longitudinal studies have been limited, likely due to the tremendous efforts needed to determine the adiponectin level, VAT and SAT at multiple time points. Specifically, there has not been a longitudinal study of lifestyle and metformin interventions to examine the correlation between changes in VAT versus SAT and changes in adiponectin in prediabetic populations. Here,

Managed by Massimo Porta.

C. Zhang · R. Zhang (✉)
Center for Molecular Medicine and Genetics, School of Medicine, Wayne State University, Detroit, MI, USA
e-mail: rzhang@wayne.edu

Present Address:
C. Zhang
Division of Geriatric and Palliative Medicine, School of Medicine, University of Michigan, Ann Arbor, MI, USA

H. Luo · F. Gao · C.-T. Zhang
Department of Physics, Tianjin University, Tianjin, China

we have investigated these correlations in participants of the Diabetes Prevention Program (DPP) [4].

The DPP is a clinical trial investigating effects of lifestyle changes or metformin versus placebo on the rate of developing type 2 diabetes [4]. All DPP participants were prediabetic, and the goals of the life style intervention were to achieve and maintain a weight reduction of at least 7 % of initial body weight, through healthy eating and exercise, and to achieve and maintain a level of physical activity equivalent to 700 kcal/week [4]. The DPP data Archive version 2.1 was obtained from the NIDDK data repository. VAT and SAT volumes were measured by CT scan at the vertebral level L2–L3 and L4–L5 in 947 participants at both baseline and 1-year follow-up [5], and subject numbers in lifestyle, metformin and placebo arms were 101, 112, 108 in men and 204, 206 and 216 in women, respectively. Because adiponectin levels were not normally distributed, the correlation between adiponectin and fat depot was examined by Spearman's rank correlation coefficients. Statistical tests were performed using SAS 9.3, and $P < 0.05$ was considered statistical significant. Results based on L2–L3 and L4–L5 were consistent, and therefore, only those of L2–L3 are shown.

First, we examined the correlation at baseline between SAT and VAT volumes with adiponectin. In men, no significant correlation was observed between adiponectin levels with either SAT or VAT (Fig. 1a, b), while in women, adiponectin was negatively correlated with SAT ($r_s = -0.154$, $P < 0.001$) and with VAT ($r_s = -0.130$, $P < 0.001$) (Fig. 2a, b).

Next, we examined the correlations between the change in adiponectin levels and the change in SAT and VAT volumes. In men, the change in adiponectin levels was highly significantly correlated with the change in both SAT ($r_s = -0.329$, $P < 0.001$) and VAT ($r_s = -0.413$, $P < 0.001$) (Fig. 1c, d). Likewise, in women, the change in adiponectin levels was also significantly correlated with the change in both SAT ($r_s = -0.294$, $P < 0.001$) and VAT ($r_s = -0.348$, $P < 0.001$) (Fig. 2c, d). Therefore, for both men and women, changes in adiponectin levels were significantly negatively correlated with changes in both SAT and VAT.

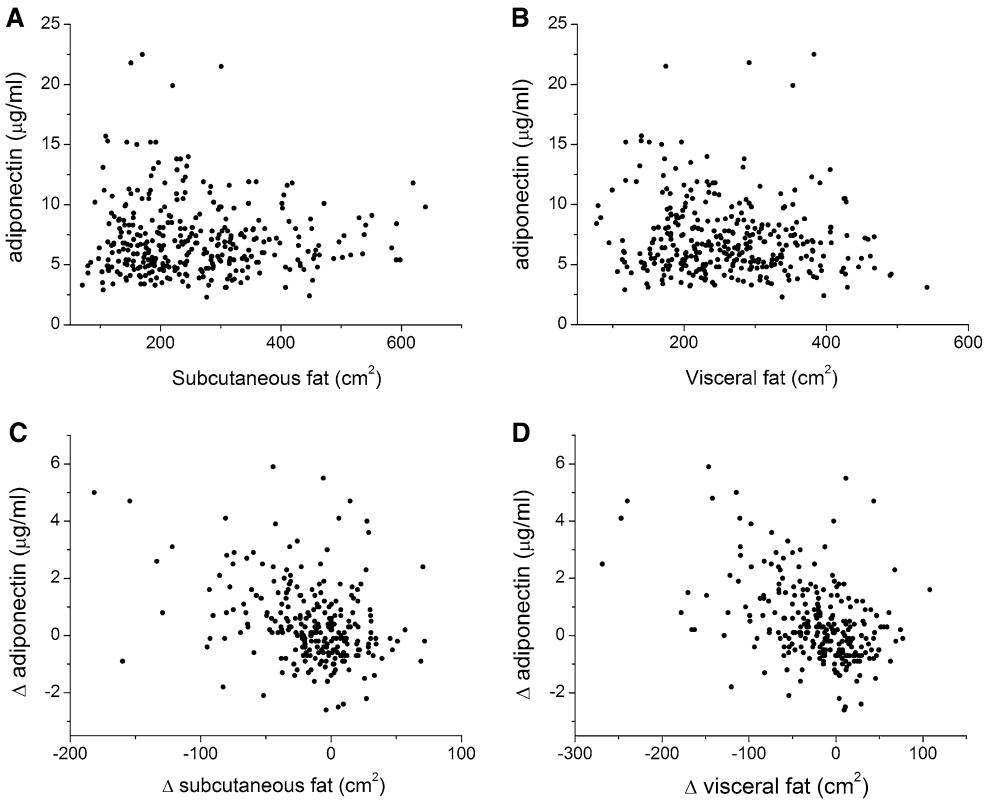

Fig. 1 Correlations between adipose tissue volume and adiponectin in male participants of the Diabetes Prevention Program. Correlations between (**a**) subcutaneous ($r_s = 0.024$, $P = 0.66$) and (**b**) visceral fats ($r_s = -0.099$, $P = 0.07$) with adiponectin levels at baseline. Correlations between the change in (**c**) subcutaneous ($r_s = -0.329$, $P < 0.001$) and (**d**) visceral fats ($r_s = -0.413$, $P < 0.001$) with change in adiponectin levels. There were 321 male participants. Adipose tissue volume was measured at baseline and 1-year follow-up by computed tomography at the L2–L3 level. $\Delta = \text{value}_{(\text{year 1})} - \text{value}_{(\text{baseline})}$, where values correspond to fat volume or adiponectin. The Spearman's rank correlation coefficient r_s is calculated

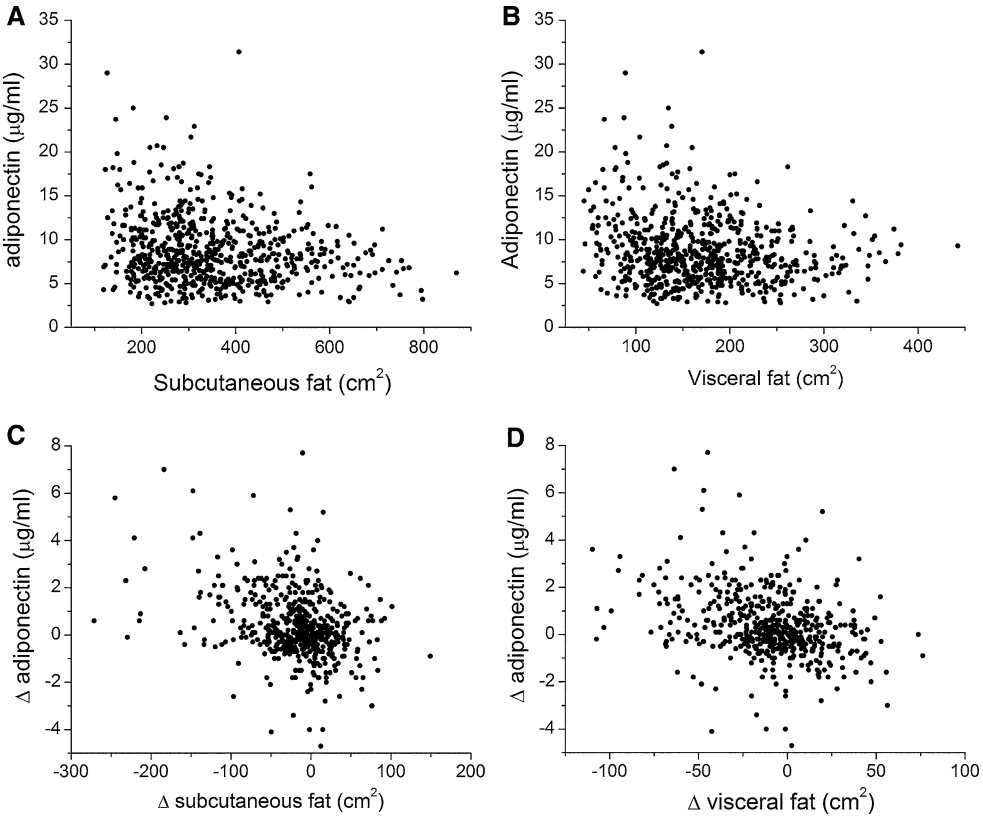

Fig. 2 Correlations between adipose tissue volume and adiponectin in female participants of the Diabetes Prevention Program. Correlations between (**a**) subcutaneous ($r_s = -0.154$, $P < 0.001$) and (**b**) visceral fats ($r_s = -0.130$, $P < 0.001$) with adiponectin levels at baseline. Correlations between the change in (**c**) subcutaneous ($r_s = -0.294$, $P < 0.001$) and (**d**) visceral fats ($r_s = -0.348$, $P < 0.001$) with change in adiponectin levels. There are 626 female participants. Adipose tissue volume was measured at baseline and 1-year follow-up by computed tomography at the L2–L3 level. $\Delta = \text{value}_{(\text{year 1})} - \text{value}_{(\text{baseline})}$, where values correspond to fat volume or adiponectin. The Spearman's rank correlation coefficient r_s is calculated

We then compared the correlations in response to lifestyle changes and metformin versus placebo. In the lifestyle arm, changes in adiponectin levels remained highly significantly correlated with changes in SAT and VAT in men ($r_s = -0.399$ and $r_s = -0.460$, respectively), and in women ($r_s = -0.372$ and $r_s = -0.396$, respectively), with $P < 0.001$ for all above correlations. In the metformin arm, the only significant correlation was between changes of adiponectin and VAT in women ($r_s = -0.299$, $P < 0.001$). In the placebo group, changes in adiponectin were negatively correlated with changes in SAT and VAT, albeit to a much lesser extent, compared to the lifestyle group. The correlation coefficients of changes in adiponectin with changes in SAT and VAT were -0.234 ($P = 0.035$) and -0.243 ($P = 0.029$) in men, and -0.250 ($P < 0.001$) and -0.192 ($P = 0.012$) in women, respectively.

Therefore, rather than the basal adiponectin concentration, which may or may not be associated with VAT and SAT, depending on age, gender and disease conditions, what are highly significantly correlated were between *changes* in adiponectin and *changes* in both SAT and VAT for both men and women. Because adiponectin is secreted exclusively from fat, in the DPP, exercise- and weight-loss-induced reduction in both SAT and VAT contributed to the increased adiponectin, an insulin-sensitizing hormone, which plays a role in delaying type 2 diabetes development in prediabetic populations.

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Conflict of interest Chao Zhang, Hao Luo, Feng Gao, Chun-Ting Zhang and Ren Zhang declare that they have no conflict of interest.

Human and Animal Rights disclosure All procedures followed were in accordance with the ethical standards of the Institutional Review Boards of Wayne State University School of Medicine and of the Detroit Medical Center, and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed consent disclosure Informed consent was obtained from all participants being included in the study.

References

1. Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, Tobe K (2006) Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. J Clin Invest 116(7): 1784–1792
2. Spranger J, Kroke A, Mohlig M, Bergmann MM, Ristow M, Boeing H, Pfeiffer AF (2003) Adiponectin and protection against type 2 diabetes mellitus. Lancet 361(9353):226–228

3. Mather KJ, Funahashi T, Matsuzawa Y, Edelstein S, Bray GA, Kahn SE, Crandall J, Marcovina S, Goldstein B, Goldberg R (2008) Adiponectin, change in adiponectin, and progression to diabetes in the Diabetes Prevention Program. Diabetes 57(4): 980–986
4. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346(6):393–403
5. Fujimoto WY, Jablonski KA, Bray GA, Kriska A, Barrett-Connor E, Haffner S, Hanson R, Hill JO, Hubbard V, Stamm E, Pi-Sunyer FX (2007) Body size and shape changes and the risk of diabetes in the Diabetes Prevention Program. Diabetes 56(6):1680–1685