Differences in Glucose Control, Insulin Sensitivity, and Body Composition Between Metabolically Healthy and Unhealthy People with Obesity

Melissa L. An, BA [a], Gordon I. Smith, PhD [b], Samuel Klein, MD [b]

[a] University of Missouri School of Medicine, Columbia, MO
[b] Washington University in St. Louis School of Medicine, Center for Human Nutrition, St. Louis, MO

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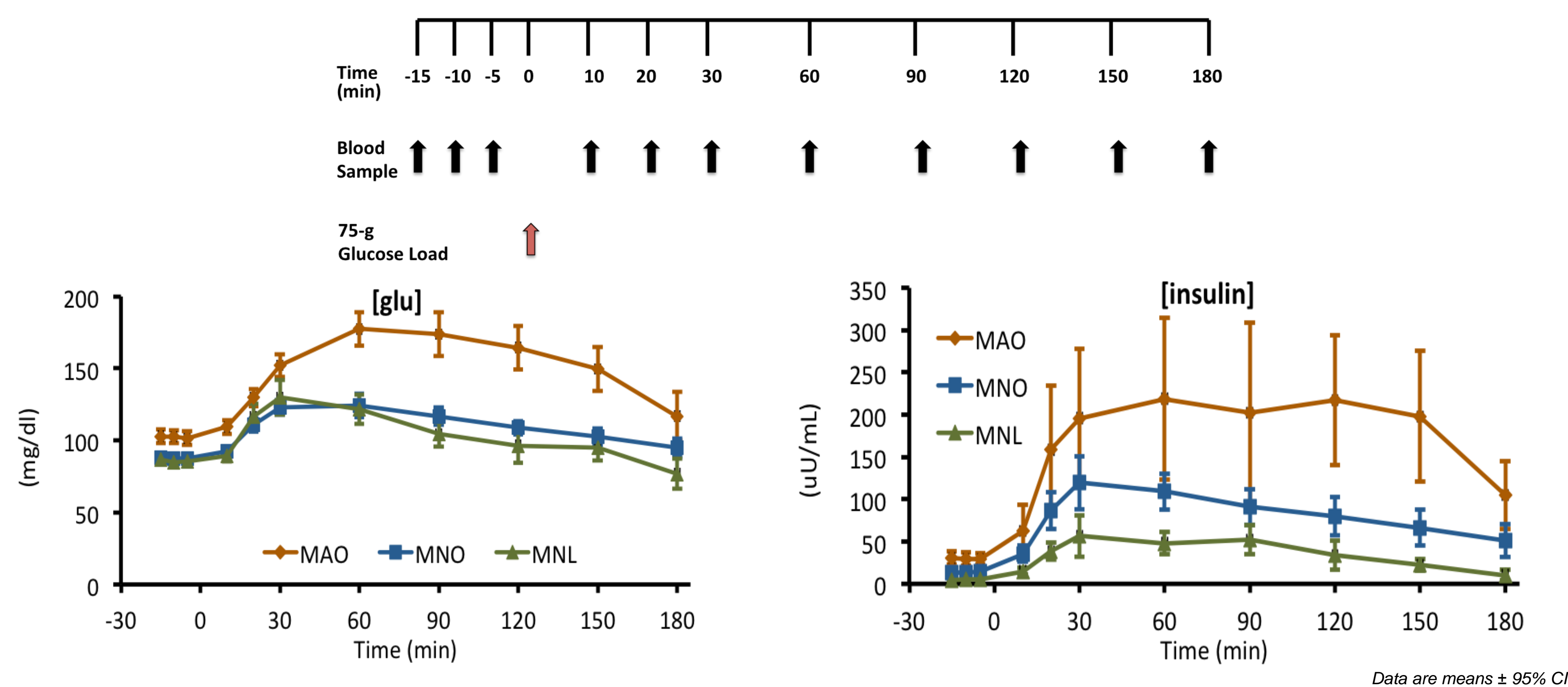
INTRODUCTION & STUDY AIMS

- Obesity is a significant risk factor for cardiometabolic complications, including type 2 diabetes and cardiovascular disease. However, approximately 25% of individuals with obesity are seemingly protected from these complications (Wildman et al. *Arch Intern Med*, 168, 1617-24, 2008).
- The purpose of this study was to provide a careful characterization of body composition and metabolic function in people who are: (i) lean and metabolically normal (MNL); (ii) obese and metabolically-normal (MNO); and (iii) obese and metabolically-abnormal (MAO).
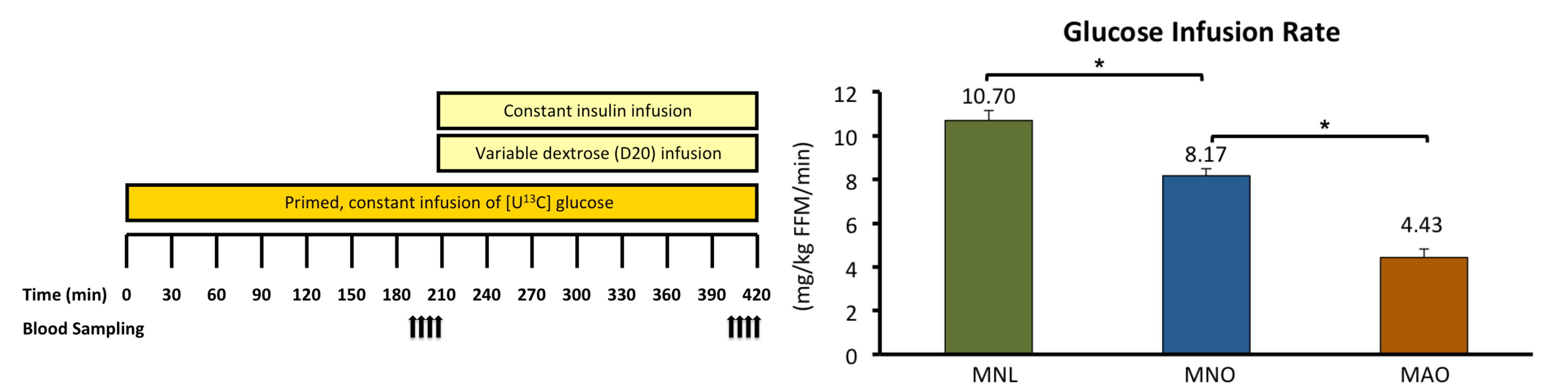
METHODS

The study is a cross-sectional analysis comparing the metabolic health between MNL, MNO, and MAO individuals. Upon screening and classification, the three groups undergo baseline testing, which includes the following measures:

1. Modified 3-hour oral glucose tolerance test (mOGTT)
2. Hyperinsulinemic-euglycemic clamp procedure
3. Dual energy X-ray absorptiometry (DXA)
4. Magnetic resonance imaging (MRI) of the abdominal region

SUBJECT CHARACTERISTICS

	MNL (n=13)	MNO (n=32)	MAO (n=23)
Age (years)	32 ± 9	35 ± 7	43 ± 9*†
BMI (kg/m^2)	23 ± 2	37 ± 4†	39 ± 5†
Waist Circumference (cm)	81 ± 6	108 ± 9†	119 ± 13*†
Systolic Blood Pressure (mmHg)	118 ± 10	122 ± 8	127 ± 9*†
HbA1c (%)	5.0 ± 0.3	5.1 ± 0.3	5.7 ± 0.7*†
Plasma Triglycerides (mg/dl)	61 ± 22	66 ± 23	125 ± 65*†
Plasma HDL (mg/dl)	67 ± 13	55 ± 14†	44 ± 11*†

HYPOTHESES

- Compared to MNL individuals, MNO individuals will have reduced insulin sensitivity.
- Compared to MNO individuals, MAO individuals will have poorer glucose control and insulin sensitivity as well as increased intra-abdominal adipose tissue volume.

MODIFIED 3-HOUR ORAL GLUCOSE TOLERANCE TEST

Data are means ± 95% CI

HYPERINSULINEMIC-EUGLYCEMIC CLAMP

Glucose Infusion Rate: MNL 10.70, MNO 8.17, MAO 4.43 (mg/kg FFM/min)

Plasma Glucose Concentration (mg/dl)

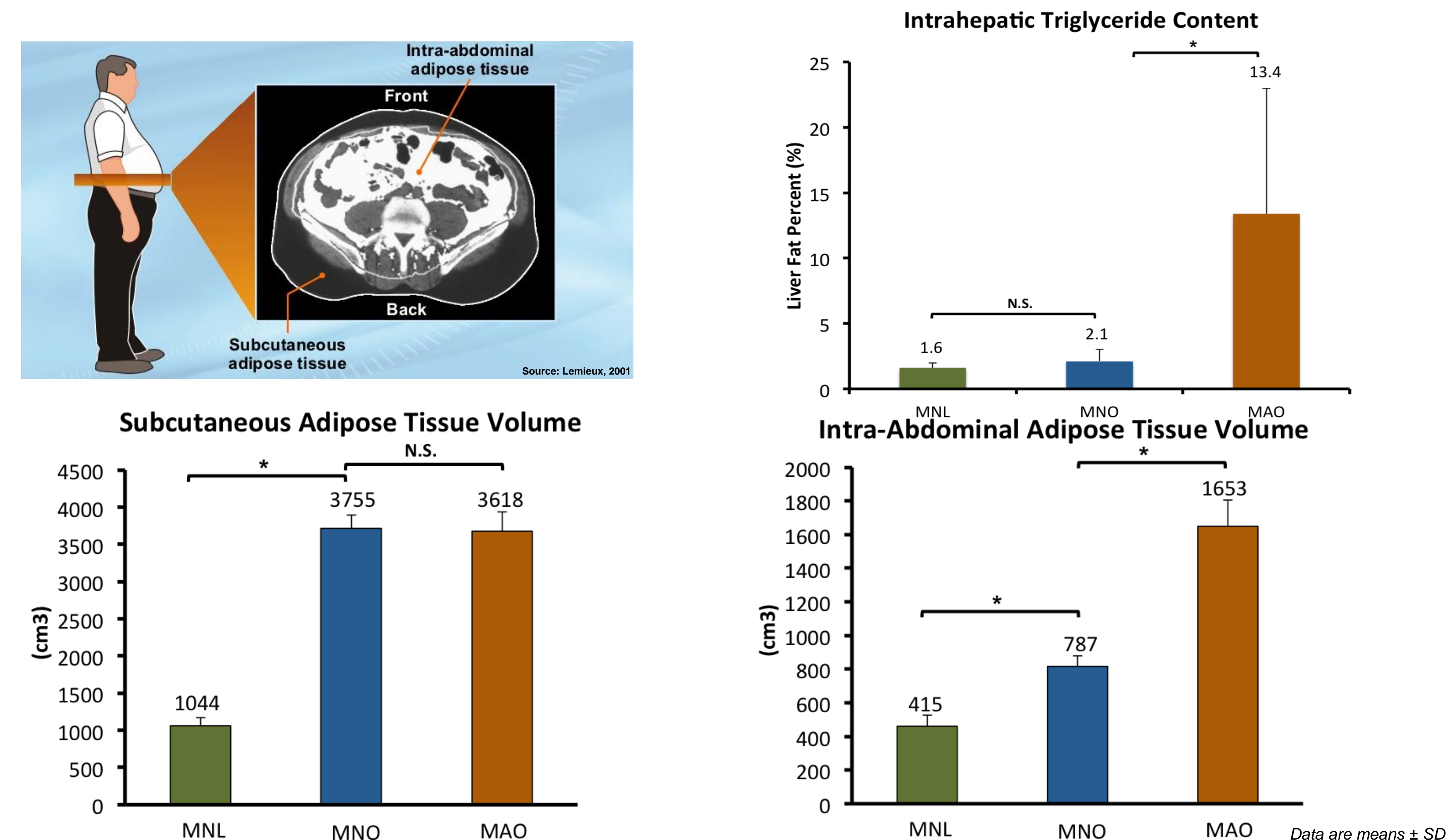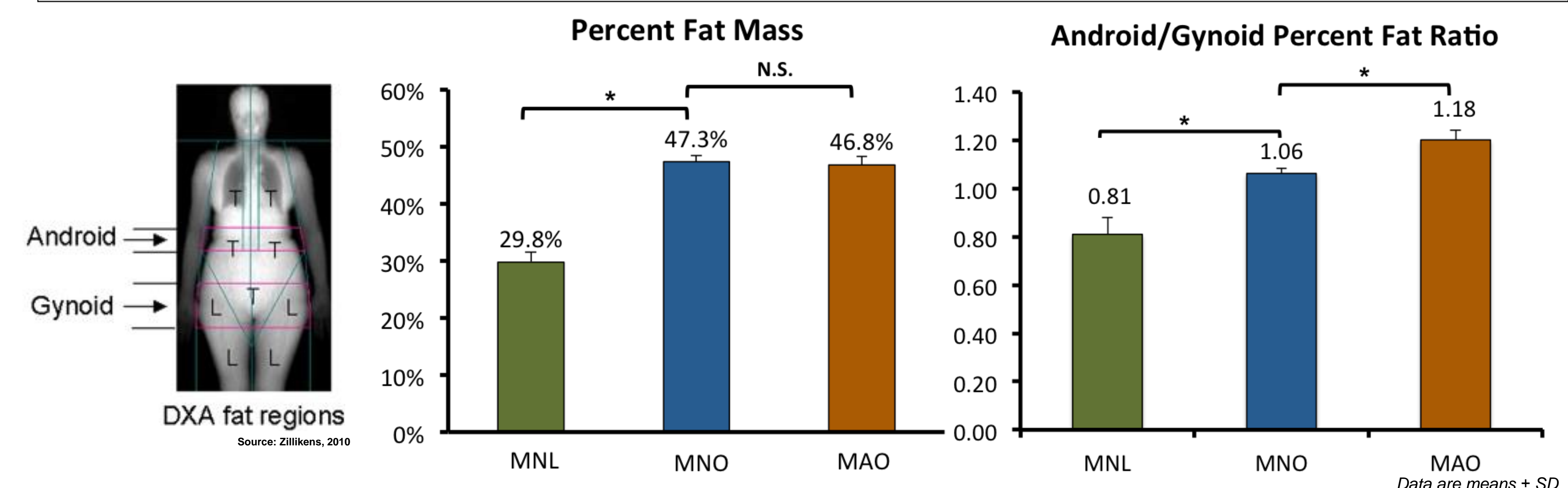|	MNL	MNO	MAO
Basal	90.1 ± 3.1	89.8 ± 1.4	101.7 ± 3.2
Clamp	99.9 ± 1.0	99.7 ± 0.7	100.9 ± 0.5

Data are means ± SD
* p<0.05 vs. MNO. † p<0.05 vs. MNL

ABDOMINAL MAGNETIC RESONANCE IMAGING

Source: Lemieux, 2001

Intrahepatic Triglyceride Content: MNL 1.6, MNO 2.1, MAO 13.4

Subcutaneous Adipose Tissue Volume (cm^3): MNL 1044, MNO 3755, MAO 3618

Intra-Abdominal Adipose Tissue Volume (cm^3): MNL 415, MNO 787, MAO 1653

Data are means ± SD

WHOLE-BODY DUAL ENERGY X-RAY ABSORPTIOMETRY

DXA fat regions — Source: Zillikens, 2010

Percent Fat Mass: MNL 29.8%, MNO 47.3%, MAO 46.8%

Android/Gynoid Percent Fat Ratio: MNL 0.81, MNO 1.06, MAO 1.18

Data are means ± SD

CONCLUSIONS

- Although the glycemic responses of MNO individuals demonstrate a "metabolically healthy" state, more rigorous measures of insulin sensitivity show insulin resistance in this population, demonstrating people with MNO are insulin-resistant with respect to glucose metabolism but are able to maintain normal glycemic control by increased insulin secretion.
- Adipose tissue distribution is a marker of metabolic health in people with obesity, as greater intra-abdominal adipose tissue volume and intrahepatic triglyceride content are associated with metabolic dysfunction.