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## Liver damage can be associated with deregulation of the de novo lipogenesis pathway in subjects with Non Alcoholic Fatty Liver Disease

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Introduction. Adipose tissue insulin resistance (IR) and elevated adipose free fatty acid (FFA) flux are prominent features in NAFLD. De novo lipogenesis (DNL) is up to 3-fold higher in subjects with fatty liver and is not suppressed on fasting. When DNL is stimulated, the production of saturated FAs is increased and the oxidation of FAs of any source is reduced. Both mechanisms can favor inflammation and IR.

Aim. We measured FFA flux/composition and used a surrogate index of DNL (DNLi) to evaluate their relationship with histological features in a group of non-diabetic subjects with biopsy-proven NAFLD.

Materials and Methods. Hepatic and adipose tissue-IR indices were derived from [2H5]glycerol and [2H2] glucose kinetics in a group of non-diabetic NAFLD patients in the basal state (n=40) and after a 4h oral glucose load test (n=20). Gas chromatography mass spectrometry was used to assess FFAs composition. DNLi was derived as the ratio palmitic/linoleic acid.

Results: Fasting plasma glucose/insulin, lipid profile, hepatic/adipose tissue IR indices and DNLi were similar in the two groups. Fasting DNLi was associated with triglycerides (TG) and FFAs levels and with adipose tissue IR (r=0.597, r=0.330 and r=0.394, respectively). Among histological features, fasting DNLi significantly correlated with steatosis (r=0.364, P=0.02) and NAS score (r=0.306, P=0.05). After the glucose load, TG levels initially increased despite elevated insulin levels, suggesting a significant contribution of DNL. Accordingly, DNLi consensually increased with TG levels (r=0.749, P<0.005) and was significantly related to the degree of fibrosis (rs=0.514, P=0.02).

Conclusions. Oral glucose load is associated with changes in DNL and hepatic triglyceride synthesis that can favor liver fibrosis in patients with NAFLD.

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