# Acute exercise leads to increased levels of plasma carnosine and carnosine-acrolein conjugates in humans

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**Introduction** Carnosine (β-alanyl-L-histidine) is mainly synthesized and stored in skeletal muscles where it exerts different functions (e.g. quencher of damaging aldehydes such as acrolein). Predominantly based on animal studies, a paracrine or endocrine role has already been proposed, implying a release of carnosine from contracting myocytes into the circulation. However, this effect may be hindered in humans due to the highly active carnosine-degrading enzyme serum carnosinase (CN1) in the circulation. This study aimed to investigate the effect of acute exercise on circulating carnosine and carnosine-acrolein (carnosine-propanal and carnosine-propanol) levels in subjects with low and high CN1 activity.

**Methods** Nine subjects with low (1.51 ± 0.62 µmol/ml/h) and seven subjects with high (3.34 ± 0.50 µmol/ml/h) CN1 activity participated in a randomized crossover trial where they performed cycling exercise for 1h at 40% of $P_{max}$ or remained at rest. Plasma samples were collected before (0'), during (30') and after (60' and 90') exercise or rest and carnosine(-acrolein) concentrations were determined using LC-MS/MS. A 2x4x2 Repeated Measures MANOVA was performed with condition (exercise vs rest) and time (0', 30', 60', 90') as within-subjects factors and CN1 activity (low vs high) as between-subjects factor.

**Results** Exercise increased plasma carnosine after 60 minutes in subjects with high ($p = 0.006$), but not in subjects with low ($p = 1.000$) CN1 activity. A similar exercise-induced increase for carnosine-propanal and -propanol was found (PAL: $p < 0.001$; POL: $p < 0.001$), being more pronounced in the high (PAL: $p < 0.001$; POL: $p = 0.004$) compared to the low (PAL: $p = 0.051$; POL: $p = 0.036$) CN1 activity group.

**Conclusions** We are the first to show an increase of plasma carnosine and carnosine-acrolein conjugates in response to aerobic exercise in humans. Strikingly, the increase was more pronounced in subjects with high CN1 activity compared to subjects with low CN1 activity. These data suggest an active release of carnosine and carnosine-acrolein conjugates from skeletal muscle into the circulation. Given the therapeutic potential of carnosine, this novel paracrine or endocrine mechanism may have important pathophysiological implications.