LS25-009 - Effects of metyrapone treatment on cardio-metabolic risk and chronobiology in patients with mild autonomous cortisol secretion

Zusammenfassung

Mild autonomous cortisol secretion (MACS) is the most common hormonal abnormality in patients with adrenal adenomas. MACS has been associated with an increased morbidity and mortality, mainly because of cardio-metabolic diseases. Despite its high prevalence, therapeutic management of MACS is not well defined and evidence on the potentially beneficial effects of medical treatment is lacking. Pharmacological treatment options might be especially relevant for patients ineligible for surgery, but could also be a useful tool for identifying patients (i.e. responders to medical therapy), who are most likely to benefit from subsequent surgical intervention to guide individual treatment decisions.

Chronotherapy might be a promising approach for the medical treatment of MACS with the aim to normalize circadian cortisol rhythmicity, as previous studies have shown abnormally elevated cortisol levels late at night. We recently investigated the impact of treatment with evening doses of metyrapone, a selective inhibitor of adrenal cortisol production, in 15 patients with MACS in a proof-of-concept study. Preliminary results indicate substantial improvements in hepatic lipid metabolism, glucose homeostasis, blood pressure and inflammation.

The aim of this proposal is to confirm these promising cardio-metabolic effects in a randomized, placebo-controlled, cross-over trial (Aim 1). In addition, as cortisol is key for the rhythmic expression of circadian signals, we aim to identify disease-specific changes in the individual chronobiology profile (Aim 2).

We will combine state-of the art cardio-metabolic phenotyping with an in depth-characterization of the individual chronobiology applying a multi-disciplinary protocol.

The results of our study will have a direct impact on routine clinical care and might pave the way for future therapeutic strategies for patients with MACS towards an individualized, patient-centered treatment.

Wissenschaftliche Disziplinen:
Endocrinology (70%) | Chronobiology (20%) | Laboratory diagnostics (10%)

Schlagworte:
MACS (mild autonomous cortisol secretion)adrenal adenomachronotherapymetyraponehypercortisolismcardio-vascular endocrinology

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Status: Laufend (01.09.2026 – 31.08.2030)

GrantID: 10.47379/LS25009

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https://www.wwtf.at/funding/programmes/ls/LS25-009/