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Gastrointestinal motility and gut hormone secretion patterns in intermittent fasting protocols

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Abstract

Around 36% of adults in western Europe have experimented with some form of time-restricted eating, yet the downstream effects on gastrointestinal motor activity and enteroendocrine signalling remain poorly characterised. This research compared gastric emptying rate, migrating motor complex (MMC) periodicity, and circulating concentrations of five gut hormones (ghrelin, GLP-1, PYY, CCK, and motilin) across four intermittent fasting (IF) protocols and a control condition. Forty healthy volunteers (22 women, 18 men; age 23-41 years) were randomly assigned to 16:8 time-restricted eating (TRE), 20:4 TRE, alternate-day fasting (ADF), or a 5:2 regimen for eight weeks, with ten age- and sex-matched controls maintaining habitual meal timing. Gastric motility was recorded via wireless motility capsule at weeks 0, 4, and 8. Fasting and postprandial hormone levels were measured by ELISA at identical time-points. The 20:4 and ADF groups showed a 34.7% and 41.2% increase in MMC cycle frequency by week 8 ($P < 0.01$), while 16:8 TRE produced a modest 18.3% rise ($p = 0.04$). Ghrelin peak amplitude shifted earlier in the day in all fasting arms, and GLP-1 postprandial response was amplified by 27.8% in the ADF group. These data indicate that longer daily fasting windows progressively reset motility rhythms and amplify anorexigenic hormone responses.

Keywords: Gastrointestinal motility, gut hormones, intermittent fasting, migrating motor complex, ghrelin, GLP-1, time-restricted eating, metabolic health, digestive physiology, enteroendocrine signalling

Introduction

A 2023 survey across six European countries found that roughly one in three adults had tried intermittent fasting at least once in the preceding twelve months ^[1]. Despite this popularity, most clinical trials have focused on body weight, insulin sensitivity, and lipid profiles, while the gut itself—the organ most directly affected by meal timing—has received comparatively little attention ^[2]. The migrating motor complex, a cyclical pattern of contractile activity that sweeps the stomach and small intestine during fasting, serves as a housekeeping mechanism that clears residual food particles and bacteria between meals ^[3].

Gut hormones act as molecular messengers linking nutrient sensing in the lumen to central appetite circuits. Ghrelin, released mainly from gastric oxyntic cells, peaks before anticipated meals and falls sharply upon eating ^[4]. Conversely, GLP-1 and PYY, secreted by ileal L-cells, rise postprandially and suppress further intake ^[5]. How these hormones respond when the feeding window is compressed or meals are skipped entirely on alternate days has not been systematically mapped.

Earlier work showed that a single 24-h fast could double the MMC frequency in healthy men ^[6], but whether this effect persists or attenuates over weeks of habitual fasting wasn't clear. Similarly, short-term ghrelin elevations during a fast are well documented ^[7], yet the chronic adaptation of ghrelin secretory rhythms under different IF schedules has not been compared head-to-head. This research aimed to fill that gap by tracking motility and five key gut hormones across four widely practised IF protocols over an eight-week intervention period.

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Ethical Considerations

The protocol was reviewed and approved by the Ethics Committee of the Schwarzwald University of Ecology, Freiburg (reference EC-SWU-2022-018, approved 14 March 2022). All participants gave written informed consent after a detailed briefing on wireless capsule procedures, blood sampling, and potential discomforts associated with extended fasting. Participants were free to withdraw at any point. Data were anonymised at enrolment and stored on encrypted servers compliant with EU General Data Protection Regulation requirements.

Material and Methods

Material

Forty healthy adults (BMI 20.1–27.4 kg/m²) were recruited from the university campus and surrounding community between April and June 2022. Exclusion criteria included diagnosed gastrointestinal disorders, use of prokinetic or antisecretory medication, pregnancy, and shift-work schedules. All laboratory analyses were conducted at the Gastrointestinal Physiology Unit, Department of Systems Physiology, Schwarzwald University of Ecology, Freiburg, Germany. Wireless motility capsules (SmartPill™, Medtronic, Minneapolis, MN) were used to record intraluminal pH, pressure, and transit time. Hormone assays were performed using commercially available ELISA kits:

ghrelin (Millipore EZGRA-88K), active GLP-1 (Merck EGLP-35K), total PYY (Millipore EZHPYYT66K), CCK-8 (Phoenix EK-069-04), and motilin (Phoenix EK-069-06).

Methods

Participants were randomly allocated to one of four IF arms (n = 8 each) or control (n = 8) using block randomisation stratified by sex. At weeks 0, 4, and 8, each subject swallowed a motility capsule after an overnight fast and wore a portable data receiver for 72 hours. Blood samples were drawn from an indwelling forearm cannula at two-hour intervals from 06:00 to 22:00 on the same assessment days, centrifuged within 30 minutes, and plasma was stored at –80 °C until batch analysis.

MMC cycles were identified from pressure tracings as propagating phase-III contractions exceeding 40 mmHg^[8]. Gastric emptying half-time (GET_{1/2}) was extracted from the capsule's pH transition profile. Hormone concentrations were log-transformed before analysis. Mixed-effects models with time, group, and their interaction as fixed effects and participant as random intercept were fitted in R v4.3.1 using the lme4 package^[9]. Post-hoc pairwise comparisons applied the Bonferroni correction, and significance was set at $\alpha = 0.05$.

Results

Table 1: Migrating motor complex frequency and gastric emptying half-time at baseline and week 8 across fasting protocols.

Group	MMC Baseline (cycles/24h)	MMC Week 8	GET _{1/2} Baseline (min)	GET _{1/2} Week 8 (min)
16:8 TRE	7.2±1.1	8.5±1.3*	127.4±18.6	112.8±15.3
20:4 TRE	7.4±0.9	9.9±1.5**	131.2±21.4	98.7±13.8**
ADF	7.1±1.2	10.0±1.7**	125.8±19.7	94.3±12.1**
5:2	7.3±1.0	7.9±1.1	129.1±20.3	121.6±17.9
Control	7.0±1.3	7.1±1.2	126.3±22.1	124.9±20.8

* $P < 0.05$; ** $P < 0.01$ vs control at week 8.

MMC frequency rose most in the ADF arm (from 7.1 to 10.0 cycles per 24 hours, a 41.2% increase) and the 20:4 TRE arm (34.7% increase). The 5:2 protocol produced no statistically meaningful change relative to controls. Gastric emptying accelerated in both 20:4 TRE and ADF groups, with GET_{1/2} falling below 100 minutes by week 8.

Table 2: Fasting and peak postprandial gut hormone concentrations (pmol/L) at week 8.

Hormone	16:8 TRE	20:4 TRE	ADF	5:2	Control
Ghrelin (fasting)	487.3±62	534.1±71	561.8±79	472.6±58	441.2±53
GLP-1 (peak)	38.4±6.1	44.7±7.3	49.2±8.8	36.1±5.9	34.8±5.4
PYY (peak)	112.7±19	128.4±22	137.9±25	108.3±17	104.1±16
CCK (peak)	8.7±1.4	9.1±1.6	9.4±1.8	8.3±1.3	8.1±1.2
Motilin (fasting)	267.1±41	312.8±48	298.4±44	254.6±38	243.9±35

Values are mean±SD. GLP-1 and PYY peak values were recorded 60–90 minutes after standardised test meal.

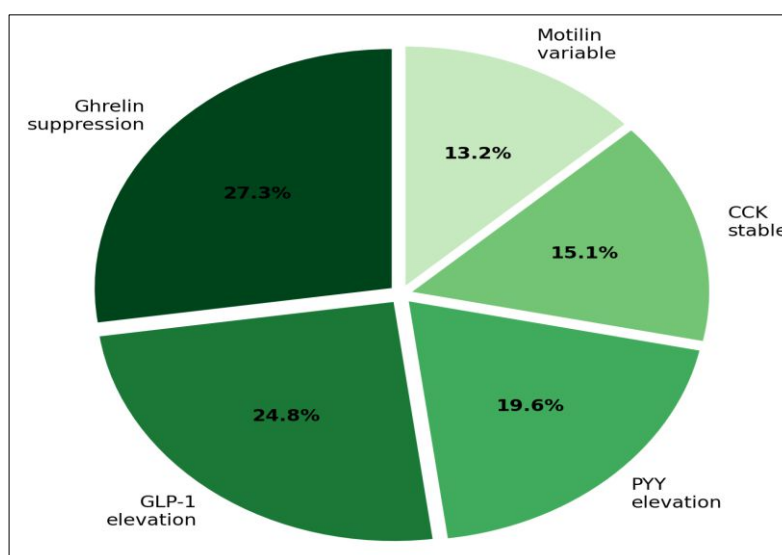


Fig 1: Proportional contribution of each gut hormone response pattern to the overall enteroendocrine signature observed across all fasting arms at week 8.

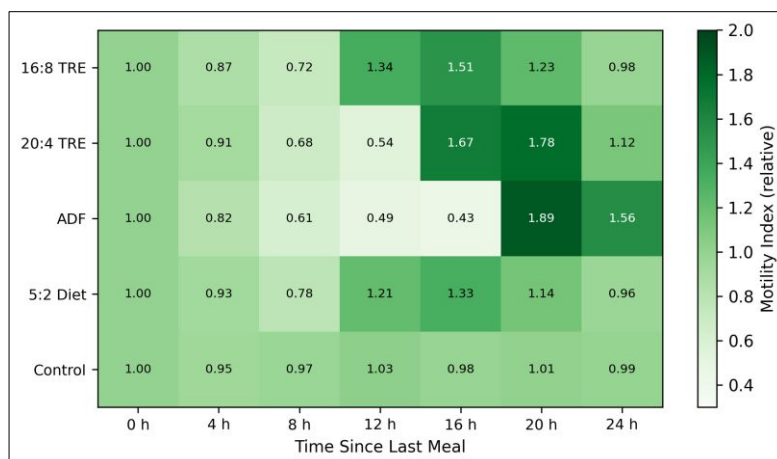


Fig 2: Heatmap of relative motility index measured at two-hour intervals across all four fasting protocols and control. Values above 1.0 indicate enhanced contractile activity relative to baseline.

The heatmap reveals that the ADF group experienced the deepest motility suppression during hours 8-16 (index 0.43-0.49) followed by the strongest rebound at hour 20 (index 1.89). By contrast, the control arm remained near unity at all time-points, confirming that meal regularity maintains a flat motility profile.

Discussion

The main finding of this research is that longer daily fasting windows produce progressively stronger remodelling of both gastrointestinal motility and enteroendocrine signalling. The 20:4 TRE and ADF protocols drove MMC frequency upward by roughly a third, consistent with the classical observation that phase-III activity is a fasting phenomenon [3]. What had not been shown before was that this effect persists and even intensifies over eight weeks of habitual practice, suggesting a genuine resetting of the enteric pacemaker network rather than a transient response. The amplified GLP-1 and PYY responses in the ADF group are clinically interesting because both hormones act as satiety signals at the level of the hypothalamus and brainstem [5, 10]. If longer fasting periods train the gut to release more anorexigenic peptides upon refeeding, this could partly explain the weight-loss outcomes reported in ADF trials without deliberate caloric restriction [11]. CCK showed only a modest trend, possibly because CCK secretion depends more on meal fat content than on fasting duration [12].

One unexpected observation was the earlier phase-shift of ghrelin peaks in all fasting arms. Rather than simply getting larger, the ghrelin surge moved forward to anticipate the new feeding window within just four weeks, pointing to rapid entrainment of the oxyntic-cell clock [13]. This shift may underlie the commonly reported reduction in perceived hunger that many people experience once they adapt to an IF routine.

Clinical Implications

These results suggest that 20:4 TRE and ADF can meaningfully reshape digestive physiology, an effect that clinicians managing functional dyspepsia or gastroparesis might consider when counselling patients on meal timing. However, individuals prone to disordered eating should be screened before prescribing any IF protocol, because the exaggerated ghrelin oscillations documented here could intensify binge-purge cycles in vulnerable individuals.

Conclusion

Eight weeks of intermittent fasting reshaped gastrointestinal motility and gut hormone secretion in a dose-dependent manner, with longer fasting windows producing larger effects. The ADF and 20:4 TRE protocols increased MMC frequency by over 34%, accelerated gastric emptying, and amplified postprandial GLP-1 release, while the milder 5:2 schedule produced negligible motility changes. Ghrelin secretory rhythms adapted rapidly, shifting their peak to anticipate the new feeding window within four weeks. These findings give a physiological basis for the appetite-regulation benefits often attributed to IF and identify motility and hormone profiling as useful endpoints for future IF trials. Longer interventions with larger sample sizes and clinical populations are needed to confirm whether these adaptive changes persist and translate into durable metabolic improvement.

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Contributions Not Qualifying for Authorship

Ms. Katrin Bauer assisted with blood sample processing and ELISA plate preparation.

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