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Caffeine can reduce insulin sensitivity in humans

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1. ABSTRACT

The analyzed study evaluated whether caffeine reduces the ability of insulin to promote glucose uptake into cells. In a randomized, double-blind, crossover design, 12 healthy volunteers received either caffeine or a placebo intravenously; insulin sensitivity was measured using the hyperinsulinemic-euglycemic clamp, the gold-standard method for quantifying the effect of insulin. Caffeine reduced insulin sensitivity by 15% compared to the placebo.The research contributes to the passage from "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, which states that a single dose of caffeine can acutely reduce insulin sensitivity. Independent crossover studies, a meta-analysis of seven trials, and experiments with caffeinated coffee confirm a lower efficiency in glucose control in the short term. However, these data do not prove that habitual coffee consumption causes chronic insulin resistance: a 24-week trial on coffee did not detect a significant change in insulin sensitivity.

ONLINE ARTICLE

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MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was simple but important: can caffeine, a stimulant found in coffee and many other beverages, temporarily make insulin less effective in healthy individuals? The authors' hypothesis was that caffeine reduces insulin sensitivity, which is the body's ability to use insulin to move glucose from the blood into tissues, especially in the muscles.This publication is relevant to section 4.16 of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi because it precisely documents the acute segment of the narrative: after a single exposure to caffeine, the body's response to insulin decreases. It does not, however, examine habitual coffee consumption, future risk of diabetes, sleep quality, or the activation of the hypothalamic-pituitary-adrenal axis.The study can therefore demonstrate an immediate metabolic effect of caffeine administered under controlled experimental conditions. It cannot establish whether this effect persists in the long term, whether it occurs with every method of coffee intake, or whether it alone causes metabolic disease.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors enrolled 12 healthy volunteers in a randomized, double-blind, crossover study. Randomized means that the order of treatments was assigned by chance; double-blind indicates that neither the participants nor the researchers in charge of the assessments knew which treatment was received; crossover means that each participant received both caffeine and a placebo at different times, acting as their own control.Caffeine or the placebo were administered intravenously. Insulin sensitivity was measured using a hyperinsulinemic-euglycemic clamp: insulin is intentionally kept high, while glucose is infused as needed to keep glycemia stable. If less glucose needs to be infused, it means that the tissues are less responsive to insulin.The authors also measured insulin, catecholamines (hormones of the acute stress response, including adrenaline and noradrenaline), free fatty acids, and hemodynamic parameters, such as blood pressure. In a second protocol, identical according to the available abstract, 10 healthy subjects received dipyridamole, a drug that inhibits adenosine reuptake. This information is not reported in the available material: caffeine dose, detailed demographic characteristics, inclusion and exclusion criteria, interval between sessions, and complete statistical method.

4. RESULTS

The main finding is that caffeine reduced insulin sensitivity by 15% compared to the placebo, with a statistically significant difference ($P < 0.05$). In practical terms, during the examination, the participants' tissues required less glucose from the infusion to keep glycemia stable: this indicates a reduced ability of insulin to promote glucose utilization throughout the body.After caffeine, free fatty acids in the blood also increased and remained higher compared to the placebo ($P < 0.05$). Adrenaline increased fivefold ($P < 0.0005$); noradrenaline ($P < 0.02$) and blood pressure ($P < 0.001$) also increased to a lesser extent. These data are consistent with an acute activation of neuro-hormonal signals that can hinder insulin action.In the second experiment, dipyridamole did not change insulin sensitivity, even though it increased noradrenaline ($P < 0.01$). The authors therefore considered it less likely that the peripheral blockade of adenosine action explains the result observed with caffeine. The abstract does not report the absolute values of glucose uptake, caffeine concentrations, or the numerical magnitude of hormonal changes, other than the fivefold increase in adrenaline.

5. INTERPRETATION

The main biological significance is that, in the short term, caffeine can cause the body to use insulin less effectively. Insulin normally promotes the movement of glucose from the blood into the cells; reduced insulin sensitivity requires a greater insulin response to achieve the same effect.The analyzed study documents the segment: acute caffeine reduced insulin-stimulated glucose utilization lower insulin sensitivity. The increase in adrenaline and free fatty acids offers a possible physiological context for the result, but it does not prove that adrenaline is the sole cause of the observed reduction. The authors themselves proposed the increase in adrenaline as a possible explanation, not as a definitively proven mechanism.In paragraph 4.16 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R.

Panzironi, cortisol, the stress axis, the PI3K/AKT pathway, and the GLUT4 transporter are also mentioned. The analyzed publication does not measure cortisol, PI3K, AKT, or GLUT4. Therefore, it directly supports only the statement regarding the acute reduction in insulin sensitivity after a single dose of caffeine, not the entire hormonal and molecular chain described in the paragraph.

6. INDEPENDENT CONFIRMING EVIDENCE

The most extensive confirmation comes from a systematic review with meta-analysis that included seven randomized trials in healthy individuals. Compared to placebo, acute caffeine intake significantly reduced the insulin sensitivity index; the standardized mean difference was –2.06, with a 95% confidence interval from –2.67 to –1.44. Heterogeneity was moderate, meaning the results were not identical across studies, but the direction of the effect was consistent: lower insulin sensitivity after caffeine [1]. This evidence directly confirms the statement in the book regarding the acute effect, although it relies on generally small studies and measures that are not always directly comparable.A previous randomized, double-blind, crossover trial studied nine young, lean, sedentary men using a hyperinsulinemic-euglycemic clamp. After 5 mg/kg of caffeine, the amount of glucose cleared by the body during the clamp decreased by 24% compared to placebo: 6.38 ± 0.76 versus 8.42 ± 0.63 mg/kg of body weight per minute. Carbohydrate storage was also 35% lower. Since glucose and insulin levels were kept comparable between trials, the result directly supports a reduced tissue response to insulin [2]. The limitation is the very small sample size and the exclusively male population.A randomized trial on 10 healthy men tested whether the effect was also observable with caffeinated coffee before mixed meals, which are more similar to a real-world context. Compared to decaffeinated coffee, coffee with 5 mg/kg of caffeine increased the area under the glucose curve by 147% after a high-glycemic index meal and by 216% after a low-glycemic index meal. After the low-glycemic index meal, it also increased the area under the insulin curve by 44% and C-peptide by 36%; C-peptide reflects the body's insulin secretion [3]. Higher glycemia despite a greater insulin response is consistent with lower insulin efficiency in the short term, but the protocol does not directly measure the clamp and does not completely separate caffeine from other coffee components.In another randomized, double-blind, crossover study, 24 healthy volunteers, 12 women and 12 men, received either a placebo or 1, 3, or 5 mg/kg of caffeine before an oral glucose tolerance test. As the dose increased, the area under the insulin curve increased by 5.8% for every mg/kg and that of C-peptide by 8.7% for every mg/kg; glucose exposure also increased. The authors concluded that the worsening of insulin sensitivity began even at low doses, with no relevant differences between sexes [4]. The design reinforces the hypothesis of an acute dose-response relationship, but it measures a response after an oral glucose load and not a long-term clinical outcome.

7. CONFLICTING EVIDENCE

An important result, rather than being directly contradictory, clarifies the significance of acute evidence. In a 24-week randomized, placebo-controlled trial, 126 overweight adults with reduced insulin sensitivity consumed four cups of regular instant coffee per day or a placebo beverage. Insulin sensitivity assessed via clamp did not change significantly with coffee compared to placebo: mean percentage difference of 4.0%, 95% confidence interval from –8.3% to 18.0%, P = 0.53 [5].This study does not refute the acute result of caffeine: it actually compares the repeated consumption of a complex beverage, containing caffeine but also other substances, in a different population and over a much longer period. However, it indicates that it is incorrect to automatically transfer the acute worsening observed after a dose of caffeine to the chronic metabolic effect of coffee. Physiological adaptation, the composition of the beverage, and individual differences can modify the result over time.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication covered by the review from independent evidence. The strength of the evidence evaluates the relevance to the book's claim, not the overall effect of coffee on health.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Double-blind, crossover RCT with clamp	12 healthy volunteers; 10 subjects in the second protocol	Intravenous caffeine reduced insulin sensitivity by 15% compared to placebo.	direct confirmation	moderate
[1]	Systematic review and meta-analysis of RCTs	Seven trials in healthy subjects	Acute caffeine reduced the insulin sensitivity index compared to placebo.	direct confirmation	moderate
[2]	Double-blind, crossover RCT with clamp	9 healthy, lean, sedentary men	Caffeine reduced insulin-stimulated glucose disposal by 24%.	direct confirmation	moderate
[3]	Crossover RCT	10 healthy men	Caffeinated coffee before a meal increased postprandial glycemia compared to decaffeinated coffee.	indirect confirmation	moderate
[4]	Double-blind, crossover RCT	24 healthy volunteers, men and women	Increasing doses of caffeine increased glucose, insulin, and C-peptide responses.	indirect confirmation	moderate
[5]	Parallel, placebo-controlled RCT	126 overweight adults with reduced insulin sensitivity	Four cups of coffee daily for 24 weeks did not significantly change insulin sensitivity.	conflicting evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The acute reduction in insulin sensitivity following caffeine intake is well-supported under controlled experimental conditions. This result has been observed using the clamp technique, glucose tolerance tests, and in studies involving caffeinated coffee consumed before carbohydrate-rich meals. The potential involvement of adrenaline and free fatty acids is biologically plausible, but not definitively proven by the analyzed study. Conversely, the evidence does not allow us to conclude that habitual coffee consumption causes chronic insulin resistance: long-term effects depend on the complete beverage, the dosage, individual adaptation, and the metabolic context.

Aggiornato al 24/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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