

Start your day with a morning coffee!

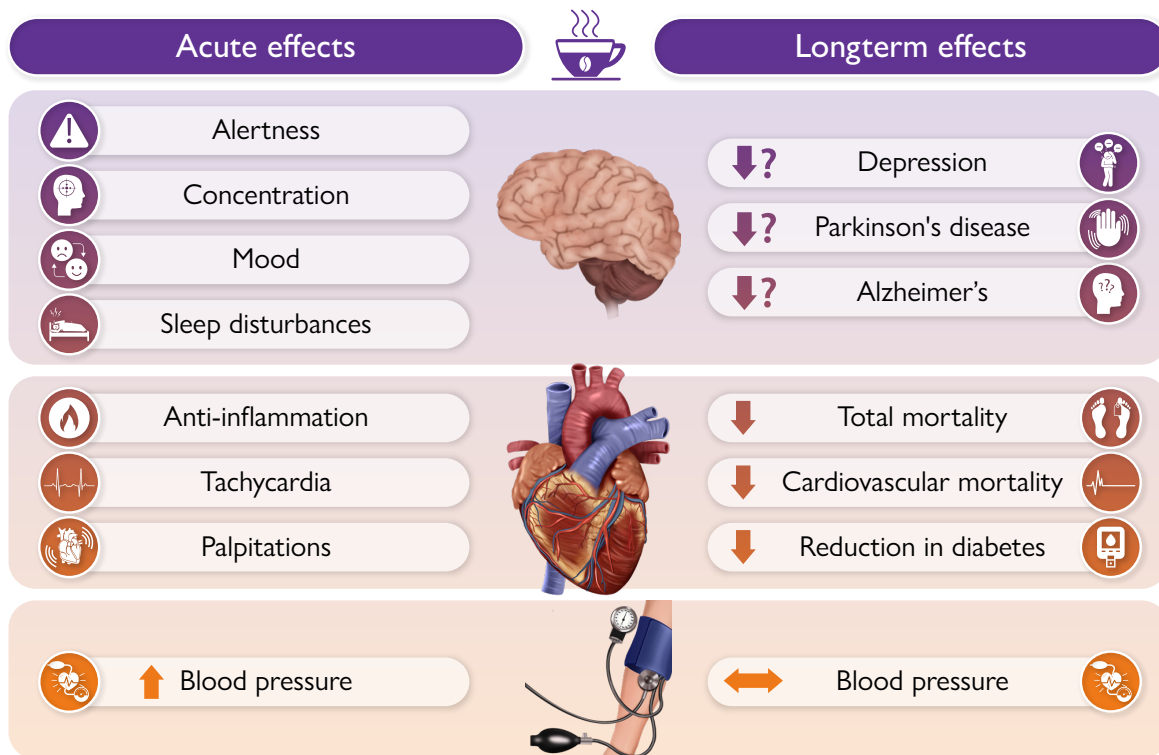
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This editorial refers to 'Coffee drinking timing and mortality in US adults', by X. Wang et al., <https://doi.org/10.1093/eurheartj/ehae871>.

Graphical Abstract

Impact of coffee on cardiometabolic and brain health



Acute (left) and longterm effects (right) of coffee consumption.

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

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Coffee is part of our daily life; it is the most commonly used commodity, with an estimated 1 billion consumers worldwide. A cup of coffee, be it an Espresso, Cappuccino, or Americano, in the morning is a must for most of us in order to get going. Indeed, caffeine, a main ingredient of coffee besides hundreds of others, has many rapid and positive actions on the brain, i.e. it enhances alertness, fosters concentration, and improves mood and well-being (*Graphical Abstract*). As the ingredients of coffee rapidly enter the brain and interfere with adenosine and its various receptors, it is not surprising that it has been shown that it reduces the risk of depression, Parkinson's disease, and Alzheimer's disease.¹

The effect of coffee beans has a long history. Indeed, as the legend goes, the goat herder Kaldi discovered coffee beans in ancient Ethiopia when he noticed that after eating berries from a certain tree, his goats no longer slept at night. Even today, coffee is mainly consumed as a stimulant by most of us as it activates the sympathetic nervous system,² wakes us up, and, in some not used to it, causes palpitations and increases blood pressure (BP). Unlike such 'virgin drinkers', habitual drinkers are protected from the stimulatory effects of coffee due to down-regulation of the response of the sympathetic nervous system with regular use. Surprisingly, this effect of coffee is at least partially independent of caffeine and due to hundreds of other ingredients that remain to be defined.² Furthermore, coffee enhances the cardiovascular response to mental stress in non-habitual coffee drinkers, with an additional increase in systolic BP, whereas in habitual drinkers that response is blunted. Caffeine alone does not exert any potentiating effect, confirming that again ingredient(s) other than caffeine are contributing to this surprising effect.³

In line with these observations, at the clinical level, moderate coffee consumption is inversely associated with the risk of heart failure, with the largest effect noted with four servings per day,⁴ recently confirmed in a machine learning analysis of several large registries.⁵ Most probably, moderate, but regular coffee drinking attenuates the massive sympathetic activation in heart failure and as such may provide some protection. In a large registry involving over 40 000 participants of the European Prospective Investigation into Cancer and Nutrition (EPIC)-Germany study, coffee consumption during almost a decade of follow-up did not affect the overall risk of chronic disease.⁶ However, both caffeinated and decaffeinated coffee consumed at a dose of four cups a day was associated with a lower risk of type 2 diabetes as compared with those drinking fewer than one cup a day. More importantly, in a large study, funded by the National Institute of Health, consumption of 4–5 cups of coffee per day was inversely associated with mortality, heart and respiratory diseases, stroke, injuries and accidents, diabetes, and infections, but not cancer.⁷

The question remained of whether it matters when coffee is consumed. In their study published in this issue of the *European Heart Journal*, Wang *et al.*⁸ analysed the time of the day when coffee is consumed in 40 725 adults from the NHANES and of 1463 adults from the Women's and Men's Lifestyle Validation Study. They noticed two distinct patterns of coffee drinking, i.e. the morning-type pattern, present in around a third of participants, and a less common all-day-type pattern present in 14% of the participants. During a median follow-up of almost a decade, and after adjustment for caffeinated and decaffeinated coffee intake, the amounts of cups per day, sleep hours, and other confounders, the morning-type, rather than the all-day-type pattern, was significantly associated with lower risks of all-cause mortality with a hazard ratio of 0.84 and of cardiovascular mortality of even 0.69 as compared with non-coffee drinkers.

Why would time of the day matter? In the morning hours there is commonly a marked increase in sympathetic activity⁹ as we wake up

and get out of bed, an effect that fades away during the day and reaches its lowest level during sleep. Thus, it is possible, as the authors point out, that coffee drinking in the afternoon or evening disrupts the circadian rhythm of sympathetic activity.¹⁰ Indeed, many all-day drinkers suffer from sleep disturbances. In this context, it is of interest that coffee seems to suppress melatonin, an important sleep-inducing mediator in the brain.¹⁰

The clinically most interesting effects of coffee drinking should be, and indeed are, long term in nature, i.e. its association with a reduced cardiovascular and total mortality as demonstrated in several association studies including that by Wang *et al.* in this issue. In this context, it may be relevant that coffee drinking blunts the sympathetic stimulating effects of mental stress. Indeed, recent studies showed that an increased activity of the amygdala due to mental stress is associated with worse long-term cardiovascular outcomes.¹¹ Thus, any modulating effect on that structure processing mental stress in the limbic system of the brain may be clinically important. Furthermore, coffee in the afternoon and evening disturbs sleep and, indeed, sleep quality and duration is an important cardiovascular risk factor. Of note, epidemiological studies showed that a sleep duration of ~8 h is optimal for cardiovascular outcomes¹² and this may be disturbed by coffee consumed later in the day.

Finally, sympathetic activation induces reactive oxygen species and in turn inflammation. The documented anti-inflammatory effects of coffee drinking therefore might be important as well;¹³ indeed, the role of inflammation for the occurrence of a cardiovascular event is well documented.¹⁴ Further, it is of interest that the circadian pattern of inflammation is reflected by higher plasma levels of C-reactive protein in the morning which may further contribute the pronounced benefits of morning compared with all day or late afternoon and evening coffee drinking.¹⁵

The strength of the study is the large number of individuals included and the long follow-up of almost a decade. Furthermore, the inclusion of a second, albeit smaller cohort and internal validation is noteworthy. Finally, the prospective nature of the data collection, as regards coffee consumption and dietary habits, is a further strength. On the other hand, these cohorts are not randomized trials, probably as nobody wanted to be in the placebo group, and the data therefore provide only associations rather than causality. Indeed, it is possible that coffee drinkers differ from non-drinkers in many aspects. Of note, dietary and lifestyle habits, in particular smoking, may affect any of the observed associations. Some may work against the hypothesis provided in the current study as coffee drinkers are more likely to smoke than non-drinkers. This may particularly be the case of all-day drinkers who may be somewhat more addicted to this habit that may annihilate the protective effects of coffee drinking.¹⁶

Be that as it may, it is unlikely that we will see a large, randomized trial over prolonged periods of time. Overall, we must accept the now substantial evidence that coffee drinking, particularly in the morning hours, is likely to be healthy. Thus, drink your coffee, but do so in the morning!

Declarations

Disclosure of Interest

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