The pros and cons of caffeine

Can caffeine actually keep you fit and healthy into old age? **Rebecca Thompson** *and* **Karen Keene** *investigate.*

STOP to think for a moment – how much caffeine do you consume in a single day? Would you be able to make it through the day without a fix of caffeine at breakfast or mid-afternoon? It's all around us, in tea, coffee, fizzy drinks, chocolate, even in flu remedies and painkillers. In a recent survey of caffeine consumption in older adults Thompson *et al.* (2003) reported that 96 per cent consumed large amounts of caffeine, with a mean daily consumption of 353mg (equivalent to nearly six cups of tea). Unlike other legal drugs, like alcohol and nicotine, there is no social stigma attached to consuming a lot of caffeine. It is even encouraged, becoming an integral part of modern society; walk down any high street and you stumble across numerous coffee shops.

In an increasingly health-conscious society the high levels of long-term caffeine consumption generate questions about potential health effects, and as with any drug there are concerns about addiction. However, there is also growing evidence that high long-term consumption of caffeine is associated with a lowered risk of cardiovascular disease and diabetes. Most interestingly, research is starting to suggest that caffeine minimises the cognitive decline associated with normal ageing: an important development given our increasingly ageing population. So is your cuppa brewing up trouble, or can it stir up the depths of your mind?

The physical action of caffeine

Caffeine, or 1,3,7-trimethylxanthine, is a pharmacologically active chemical. When consumed it causes mild central nervous system (CNS) stimulation. Caffeine is readily absorbed into the bloodstream and remains in the body for three to five hours (Lorist & Tops, 2003). The clearance rate of caffeine from the body is doubled in women who take oral contraceptives, and increased 30–50 per cent by nicotine intake. Peak plasma concentrations of caffeine generally occur 30–60 minutes after ingestion (Lorist & Tops, 2003). Caffeine passes through all biological membranes in the body, including the blood–brain barrier and the placental barrier. It is metabolised by the liver, with less than 5 per cent of ingested caffeine being recovered unchanged in urine (Lorist & Tops, 2003). Caffeine acts as a diuretic, increasing the amount of water/urine output from the body. It is also a vasoconstrictor: blood pressure is raised following ingestion.

At a cellular level, caffeine acts as a neuromodulator: its presynaptic action modifies/inhibits the release of many neurotransmitters. In particular, caffeine blocks receptors for the neuromodulator adenosine. The normal function of adenosine is to inhibit physiological activity by modulating the release of various neurotransmitters. Thus blocking adenosine's action results in CNS stimulation, which is accompanied by the release of several neurotransmitters including noradrenaline, acetylcholine and dopamine.

The highs and lows of caffeine

The release of the neurotransmitter acetylcholine following caffeine ingestion is of particular interest to the discussion of caffeine and cognition, because acetylcholine is involved in the attention, concentration, learning and memory networks in the brain. An important area of caffeine research centres on the question of whether caffeine has an effect on cognitive performance.

Interestingly, Reidel *et al* (1995) reported that caffeine has been shown to reverse the detrimental cognitive effects of scopolamine, a substance that blocks the neurotransmitter acetylcholine. They reported that performance on memory tasks improved while reaction times did not, suggesting that caffeine has the potential to act as a cognitive enhancer when levels of acetylcholine are low, rather than having its actions as a CNS stimulant alone.

Research has shown that ingestion of a low dose of caffeine is associated with increased alertness, vigilance and decreased fatigue. These effects are particularly evident in caffeine-deprived individuals (i.e. individuals who usually consume caffeine but who have abstained for a significant period). For example, on tasks requiring sustained performance, caffeine has been shown to counteract the degrading effects of sleep deprivation on cognitive function (e.g. Lieberman *et al.*, 2002). Subjectively, people who have recently consumed caffeine report being more alert and competent.

Despite increases in performance on vigilance and sustained attention there is little evidence to suggest that acute caffeine consumption is associated with better performance on higher cognitive functioning, including memory processes. This may in part be because the tests used to assess these functions cited in the literature (e.g. verbal learning tasks) are not sensitive enough to register the effects of caffeine. In a recent comprehensive review of the effects of an acute dose of caffeine on human behaviour, Smith (2002) concludes that caffeine increases alertness

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and reduces fatigue, as well as improving performance on vigilance tasks and tasks requiring a sustained response, particularly in low-arousal conditions, such as working at night. Smith states that the effects on more complex tasks are equivocal and that the results are often confounded by other variables, such as time of day.

Not all of the effects of caffeine are positive. Caffeine ingestion has several negative physical effects, including decreased control of fine motor movements (e.g. hand steadiness) and increased blood pressure and urine output (as mentioned above). Pregnant women are advised to limit caffeine intake to <300mg per day (equivalent to five cups of tea/three cups of coffee) in order to reduce the risk of low birth weights, miscarriage and stillbirths. When it is consumed in high doses caffeine can cause anxiety (see Smith, 2002), insomnia and increased sleep latency (the time it takes to fall asleep) compared with a placebo (Goldstein, 1994). However, Smith (2002) concludes that individuals are very adept at controlling their use of caffeine to maximise the positive effects and minimise the negative effects, for example by drinking coffee in the day to increase alertness, but abstaining in the evening to avoid insomnia. He concludes that the negative effects are generally only observed in 'caffeine-sensitive individuals' or under conditions of excessive intake.

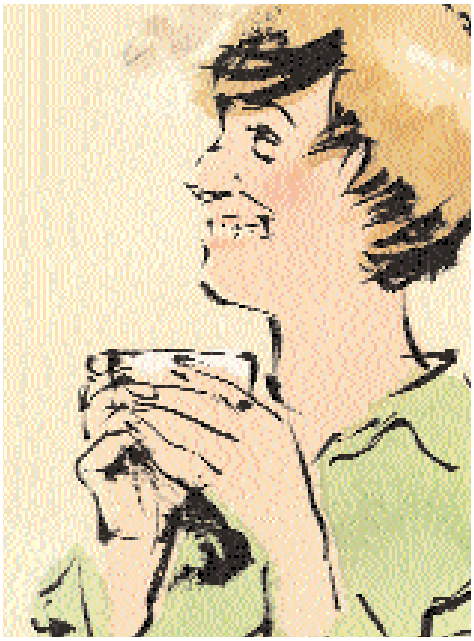
The effects of withdrawal

Caffeine has a mean half-life of 3.5 hours, and following a period of abstention, or even after a typical night's sleep, regular consumers will enter a state of 'caffeine withdrawal' (CW). CW is associated with a general negative mood, headaches, fatigue and decreased alertness. These symptoms can persist for at least seven days after the cessation of caffeine (Rogers & Dernoncourt, 1998). The state of CW is a very interesting concept that is hotly debated in caffeine research. The debate surrounds the issue of whether the cognitive effects of caffeine, such as increases in vigilance, are related to a net beneficial effect of caffeine or whether they are associated simply with a reversal of the caffeine withdrawal state.

Investigations of the CW reversal hypothesis have provided mixed results. Rogers *et al.* (2003) argue that the stimulant properties of caffeine are most likely to be a simple reversal of CW symptoms. They substantiate this claim with the finding that the effects of caffeine on cognitive tests (including reaction time tests) are less pronounced in people who do not regularly drink tea or coffee. However, others report that caffeine produces beneficial effects in both consumers and non-consumers (e.g. Smith, 2002). Further research is clearly needed.

Is caffeine addictive?

Because caffeine is a drug (albeit a legal one), there is interest into whether it has the potential to become an abused substance. The notion that caffeine is addictive is however somewhat controversial. *The Concise Oxford English Dictionary* (1995) defines addiction as 'the condition of taking a drug habitually and being unable to give it up without incurring adverse effects'. According to this definition, caffeine can be considered to be an addictive substance: individuals have particular caffeine consumption patterns and habits (e.g. making a cup of tea on arrival at work or home).



Another strong influence in a person's tendency to consume caffeine is the positive and negative reinforcement attached to the consumption of each caffeine-containing beverage. The negative reinforcement comes in the removal of bad feelings associated with the state of CW (i.e. headache and sleepiness), while the positive reinforcement is associated with the general liking of the taste of a cup of tea or the 'buzz' received from a shot of espresso. However, the argument that caffeine is addictive is not as simple as this. Nehlig (1999) states that regular caffeine consumers do not show behaviours typical of addiction – the need to gain ever-increasing doses to receive benefits. Furthermore, research indicates that moderate caffeine consumption does not act on the areas of the brain related to addiction. Nehlig and Boyet (2000) reported that in rats the shell of the nucleus accumbens, an area of the brain linked to addiction, was only activated by a very high dose of caffeine (10mg/kg). This indicates that typical daily levels of consumption will have a low addictive potential.

Is caffeine good for us?

In our health-conscious society attention inevitably turns to things that should or could be minimised or eliminated from our diets and lifestyle to promote good health. Perhaps you or someone you know will have tried to cut down on caffeine as part of a New Year's resolution. In support of this, sales of decaffeinated coffee and tea are reported to be higher in January than at any other time of year (see *www.realcoffee.co.uk*)! But are we casually discarding an elixir of youth?

Increased longevity is the result of an improved quality of life, advances in medical science and increased awareness and promotion of a healthy lifestyle (e.g. low-fat diet and regular exercise). Sadly, this longevity does not come without a heavy price – an increased incidence of diseases such as cancer, cardiovascular disease and dementia. Reassuringly, there is growing evidence from epidemiological studies that a lifetime of habitual caffeine consumption has positive effects on physical and cognitive health.

Studies concentrating on green tea, one of the richest natural sources of antioxidants (which block the harmful action of free-radicals, thus limiting cell death) have reported that a high consumption (10 or more cups a day), is associated with an overall reduced risk of developing cancer and a delay in the average age of onset of cancer (Nakachi *et*

al., 2003). This delay was 4.1 years for men and 7.6 years for women. A low consumption of green tea (less than three cups a day) was not associated with these benefits. Nakachi *et al.* (2003) additionally reported that the mean age at death among men and women drinking more than 10 cups of green tea a day was 4.3. and 3.8 years higher respectively than the mean among individuals drinking less than three cups a day. In other words, by drinking green tea you may increase your lifespan. Furthermore, Nakachi *et al.* (2000) reported that the polyphenols contained in green tea act to reduce serum lipids, thus reducing the risk of developing cardiovascular disease. It should be noted that green tea contains an average of 20mg caffeine per serving, which is considerably lower than that contained in coffee or black tea. Thus it is likely to be the antioxidant properties in the tea that have a positive effect on health over and above the effects of caffeine.

Furthermore, there are reports that long-term coffee drinking is associated with a 30 per cent reduction in the risk of developing Parkinson's disease (Martyn & Gale, 2003) and that long-term caffeine intake from

coffee and other sources is associated with a significantly lower risk of developing Type 2 diabetes (Rosengren *et al.*, 2004; Salazar-Martinez *et al.*, 2004). In the Rosengren study the risk of developing diabetes was 475 per 100,000 in women who consumed two cups of coffee or less a day compared with 267 per 100,000 in woman who consumed seven or more cups of coffee per day.

In addition to physical health benefits, caffeine has been reported to enhance cognitive health in older adults who have regularly consumed caffeine over their lifetime. For example a large population-based survey of 9003 British adults, (Jarvis, 1993) reported a dose–response trend between cognitive performance and caffeine intake in four tasks: simple reaction times, choice reaction times, incidental verbal memory and visuospatial reasoning. In other words, the more caffeine consumed over a lifetime, the better the cognitive performance in old age. The greatest benefits were observed in individuals who had consumed caffeine for the longest time.

More recently Johnson-Kozlow *et al.* (2002) reported that a higher lifetime exposure to caffeine (as opposed to current exposure) was associated with better cognitive performance in old age. This effect was highest in women aged 80 years plus. Additionally, those with regular lifetime coffee consumption (at least one cup daily for one year) performed better on cognitive tasks of memory, attention and concentration. Despite the positive results from the epidemiological studies, there have been few controlled experimental investigations of the acute doses of caffeine in older adults. This is something that we are currently investigating at the Research Institute for the Care of the Elderly.

Implications

What are the implications of the positive findings of the epidemiological studies? Should health guidelines be introduced recommending that older adults consume regular large amounts of caffeine? Clearly, before such recommendations are made, research is required to clarify the true nature of the potential 'neuroprotective'

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role of caffeine. It is unrealistic to expect that caffeine will ever provide a cure for neurodegenerative diseases such as Parkinson's or eradicate the cognitive decline associated with ageing. What is more likely is that caffeine may slow down either the onset or the progression of disease and cognitive decline, as has been reported in research on cancer and cardiovascular disease.

It is also difficult to estimate exactly how much caffeine would be needed to produce a protective benefit. Would the best option be a stable amount of caffeine across the lifespan in the form of an early intervention programme? Or would an acute dose at the beginning of the disease process help? We also need to establish whether it is the caffeine content of beverages and foods or some other active ingredient that produces the beneficial effects (e.g. the antioxidant properties of tea).

Finally it is extremely important to establish whether there are any adverse effects of high levels of consumption of caffeine-containing beverages. For example, one widely reported negative side-effect of caffeine is an increase in blood pressure (Hartley *et al.*, 2004; Waring *et al.*, 2003). This poses a real concern for health professionals as a high blood pressure is associated with an increase risk of strokes and cerebral vascular disease, which in turn increase the risk of developing conditions such as vascular dementia. Therefore there is a need for systematic investigation of whether the health benefits of high caffeine consumption can outweigh any potential detrimental health effects. But for now at least, perhaps you should sit back, relax and enjoy a nice cuppa or two!

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