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The Effects of Caffeine on the Brain: A Review

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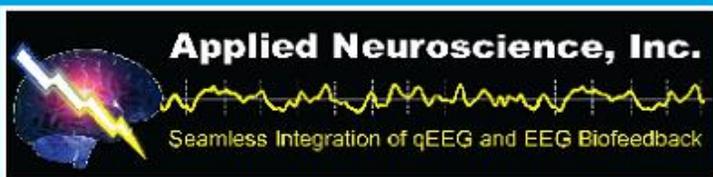
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The Effects of Caffeine on the Brain: A Review

D. Corydon Hammond, PhD

ABSTRACT. The effects of caffeine may often be overlooked in neurotherapy. However, caffeine is a potent and widely used drug which is addictive, has withdrawal symptoms associated with discontinued use, and which can produce anxiety and insomnia. It also has a rapid and profound influence on the brain, including producing increases in beta and decreases in slower brain wave activity. In contrast, during withdrawal from caffeine patients may experience increases in theta and delta, with decreases in the mean frequency of both alpha and beta. Recommendations are presented for control of caffeine use associated with EEG assessment and in neurofeedback treatment.

KEYWORDS. QEEG, EEG, caffeine, caffeine withdrawal

In recent years several studies have appeared documenting problems with anxiety, panic reactions, and insomnia resulting from the excessive use of caffeine (Chait & Griffiths, 1983; Charney, Heninger, & Jatlow, 1985; Griffiths & Woodson, 1988; Prichard, Robinson, DeBethizy, Davis, & Stiles, 1995; Uhde, 1990; Uhde, Boulenger, Vittone, Siever, & Post, 1985; Victor, Lubetsky, & Greden, 1981). Correlations have been

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found between trait-anxiety and caffeine consumption in patients with anxiety (Lee, Cameron, & Greden, 1985), generalized anxiety with phobic disorder (Boulenger & Uhde, 1982), and panic disorder (Boulenger, Uhde, Wolff, & Post, 1984). These increases in anxiety in patients with generalized anxiety disorder and panic disorder do appear to be dose related and have been validated in placebo controlled research (Bruce, Scott, Shine, & Lader, 1992), although expectancy that a placebo is caffeine does have an impact as well (e.g., Jones, Griffiths, Herning, & Cadet, 2000; Mikalsen, Bertelsen, & Flaten, 2001). Some literature also suggests that patients with generalized anxiety disorder (Bruce et al., 1992) and panic disorder are more sensitive to and also tend to consume less caffeine than normal individuals (Boulenger et al., 1984; Christensen, Bourgeois, & Cockroft, 1993; Lee, Flegel, Greden, & Cameron, 1988).

Caffeine is addictive, has been documented to build tolerance, and is associated with withdrawal symptoms that begin within one day after discontinuation and which can continue for 7 to 10 days (Silverman, Evans, Strain, & Griffiths, 1992). Withdrawal symptoms may include headaches, irritability, tension, anxiety, drowsiness, decreased alertness and problems concentrating, impaired psychomotor performance, muscle pain, fatigue and lethargy (Evans & Griffiths, 1991; Griffiths et al., 1990; Griffiths & Mumford, 1995; Silverman et al., 1992; Strain, Mumford, Silverman, & Griffiths, 1994). Studies have shown that caffeine withdrawal increases cerebral blood flow (Matthew, Barr, & Weinman, 1983; Matthew & Wilson, 1985; Jones et al., 2000) which is a likely cause of withdrawal headaches, whereas ingestion of caffeine appears to create hypoperfusion in areas where it is creating an increase in glucose metabolism (Nehlig, Pereira De Vasconcelos, Dumont, & Boyet, 1990). Reeves, Struve, Patrick, and Bullen (1995) found, and Jones et al. (2000) confirmed in a double-blind, placebo-controlled study, that there are increases in theta during caffeine withdrawal (after 20 to 22 hours without caffeine) compared with someone who regularly uses caffeine and is consuming it. The normal subjects in the Jones et al. (2000) study simultaneously reported subjective feelings of limb heaviness and a decrease in concentration. Thus, it appears that this increase in theta during caffeine withdrawal is what likely accounts for both problems concentrating and feelings of drowsiness.

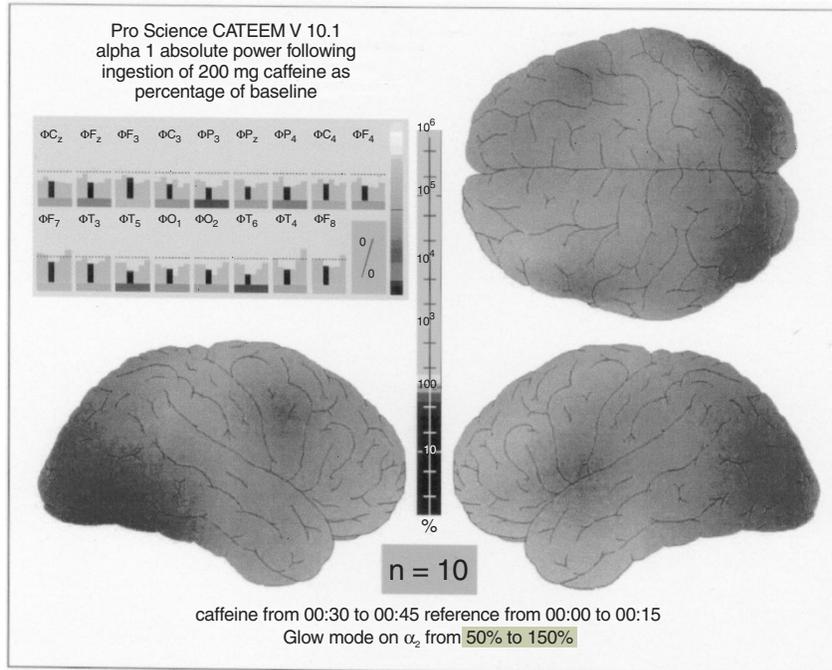
In their preliminary study, Reeves et al. (1995) found an increase in theta absolute power that was statistically significant in 92.3% of subjects experiencing caffeine withdrawal. In a recent follow-up study, Reeves, Struve, and Patrick (2002) gathered qEEG data while on caffeine, and then on days one, two, and four of caffeine withdrawal, and

then once again shortly after receiving caffeine. As withdrawal from caffeine progressed, they discovered increases in absolute power theta throughout the cortex, increases in delta absolute power frontally, and decreases in the mean frequency of both alpha and beta. There was also an increase in theta relative power, while beta decreased in relative power. Alpha and theta interhemispheric coherence increased frontally during caffeine withdrawal, but decreased in posterior areas. In contrast, theta interhemispheric coherence decreased in posterior temporal and parietal areas, and delta interhemispheric coherence decreased significantly in central and occipital areas. They found that “the greatest theta absolute power change following caffeine abstinence may occur in subjects with more severe subjective behavioral withdrawal symptoms” (p. 187). However, after receiving caffeine again, changes in alpha mean frequency returned to baseline levels within 30 minutes and all other qEEG values normalized relatively quickly.

Patrick, Reeves, and Struve (1996) discovered that individuals with diffuse paroxysmal slowing (a minor EEG dysrhythmia) in baseline resting EEGs, experienced an increased firing rate of this pattern when they were experiencing withdrawal from caffeine, but it returned to baseline or lower when caffeine was reintroduced. Although this phenomenon is clinically benign, the authors speculated that the increase in this pattern may be associated with problems with concentration and performance associated with caffeine withdrawal. Referring to implications of this finding, they concluded: “It would be important to know if clinically relevant paroxysmal EEG dysrhythmias with strong symptom expressivity also have firing rates increased by caffeine withdrawal because, if they did, such an effect could lead to adverse clinical consequences in some circumstances” (p. 83).

In a randomized, placebo controlled, double-blind crossover study, Siepmann and Kirch (2002) found that 30 minutes after ingesting the equivalent of two cups of coffee, there was a reduction of total EEG power in both hemispheres at fronto-parieto-occipital and central electrode sites, confirming previous findings (Dimpfel, Schober, & Spuler, 1993; Gilbert, Dibb, Plath, & Hiyane, 2000; Goldstein, Murphree, & Pfeiffer, 1963; Kenemans & Lorist, 1995; Newman, Stein, Trettau, Coppola, & Uhde, 1992; Saletu, Anderer, Kinsperger, & Grunberger, 1987). The reduction was more pronounced in an eyes-open than in an eyes-closed condition. This attenuation of total power, not unlike that seen with amphetamines (Goldstein et al., 1963; Saletu, Barbanoj, Anderer, Sieghart, & Grunberger, 1993), was most pronounced in the slow and fast alpha bands, as illustrated in Figure 1, as well as in slow

FIGURE 1. Eyes-Open Topographical Representations of Alpha 1 Frequencies Following Administration of 200 mg of Caffeine*



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beta. These findings are congruent with Nehlig, Daval, and Debry (1992) analysis that caffeine increases cortical activation and excitability. As cited earlier, caffeine is a vasodilator that induces cerebral hypoperfusion, which then seems to reduce EEG power.

Congruent with these findings of caffeine induced increases in beta with reduction of power in slower frequencies are the findings from event-related potential research. The amplitude of the parietal P300 has been found to be increased by caffeine (Lorist, Snel, & Kok, 1994a; Lorist, Snel, Mulder, & Kok, 1995; Ruijter, Lorist, & Snel, 1999; Ruijter, Lorist, Snel, & De Ruitter, 2000), which is associated with information processing, and the frontal P200 has also been found to increase (Lorist, Snel, & Kok, 1994b; Ruijter et al., 1999, 2000). Lorist et al. (1995) documented increased reaction time for a visually focused selec-

tive search task and in the amplitudes of the N1 and N2b in both young and old subjects after ingestion of caffeine.

In contrast, some research (Pollock, Teasdale, Stern, & Volavka, 1981; Prichard et al., 1995) found minimal or no effects from caffeine, or that it increased power (Etevenon et al., 1986; Hasenfratz & Battig, 1994), but this may be due to differences in dose (and in resting EEG versus vigilance controlled EEG), and recent research (Watters, Martin, & Schreter, 1998) has revealed a nonlinear dose-response relation between caffeine dose and arousal, much like the Yerkes-Dodson Law that predicted a negative relationship between arousal and performance.

The half-life of caffeine is estimated to be 3 to 8 hours (Rowland & Tozer, 1980), and thus, caffeine intake after lunch time has the potential to make it more difficult to fall asleep. When 100 mg of caffeine was administered at bedtime, it was found to prolong sleep latency, reduce sleep efficiency and stage 4 (NREM) sleep, and it reduced delta power density (Karacan et al., 1976; Landolt, Dijk, Gaus, & Borbely, 1995; Nicholson & Stone, 1980). However, the EEG during sleep seems to be more sensitive to caffeine than is generally imagined because Landolt et al. (1995) found that the equivalent of one to two cups of coffee in the early morning still affected sleep EEG 16 hours later! Although the sleep effects were rather small, they found that caffeine in the early morning nonetheless affected sleep propensity and the spectral power density in very slow delta (.25-.5 Hz). Thus, whenever we are screening new patients who have problems with anxiety, panic, or insomnia, it is important to inquire about caffeine intake.

Christensen et al. (1993) examined a normal individual who was prone to experiencing some anxiety after consuming caffeine. They administered the Profile of Mood States and gathered EEG on this woman prior to consuming 300 mg of caffeine. She demonstrated a slight hand tremor and a slight increase in tension. She was used to consuming a very modest amount of caffeine daily (75 mg). She then went two weeks without any caffeine and was again administered 300 mg, with testing and EEG being gathered beforehand and at 30 and 90 minutes afterwards. She experienced a full blown, five-minute panic attack at about 90 minutes after being given caffeine. As this occurred she experienced a dramatic increase in delta (with smaller increases in theta and beta) accompanied by a decrease in alpha. These changes occurred throughout the cortex, but the greatest increase in delta occurred in the left hemisphere. This finding supported earlier reports of increased delta being associated with panic reactions (Fink, Taylor, & Volavka, 1969; Knott, Chaudry, & LaPierre, 1981; LaPierre, Knott, & Gray,

1984), and is consistent with reports of panic attacks occurring in delta sleep (Lesser, Poland, Holcomb, & Rose, 1985; Mellman & Uhde, 1990). Newman, Stein, Trettau, Coppola, and Uhde (1992) reported that delta was increased in normal subjects and in panic disorder patients following administration of oral caffeine.

Bruce et al. (1992) discovered that in patients with generalized anxiety disorder or panic disorder (compared to control subjects), caffeine produced significantly less of a decrease in alpha activity and a greater decrease in N1-P2 auditory evoked potential amplitude. Hasenfratz and Battig (1994) found that increasing doses not only increased anxiety and wakefulness in normal coffee drinkers, but that it increased the dominant beta frequency and with a high dose, increased the dominant alpha frequency significantly above placebo. Similarly, Newman et al. (1992) documented that caffeine reduced theta, slow alpha (8.6-10.5 Hz) and slow, medium and fast beta amplitude, and increased the peak frequency of occipital alpha. Etevenon et al. (1986, 1988) and Bruce et al. (1986) likewise found caffeine increased mean alpha frequency and reduced alpha power, and the latter found decreased beta power as well.

In conclusion, caffeine (and caffeine withdrawal) certainly has a rapid and profound influence on the brain. Effects of caffeine must be controlled in doing EEG and qEEG assessments. Having reviewed this literature, it is my conclusion that we can run into problems in obtaining accurate assessments when caffeine is consumed, particularly in significant doses, in the few hours immediately before a qEEG and also if a regular caffeine user is kept from using caffeine for a significant period of time (e.g., 12 to 24 hours or longer). There is no data available concerning whether caffeine consumption was restricted for particular lengths of time in subjects tested for normative databases. David Kaiser (personal communication, May 31, 2002) indicated that in the SKIL database, they asked about caffeine use in the past 24 hours, but never analyzed it. Robert Thatcher (personal communication, May 30, 2002) indicated that in the NeuroGuide program with the updated Lifespan database, "children from 2 months of age to 18 years of age were totally free of caffeine as far as we can tell," and these ages represent about 75% of the database. The remaining adults provided detail in questionnaires about their diet and coffee intake, but this information is not readily available. No response was obtained to a query of the Nx Link database.

Caffeine is a potent drug to which a large number of people are at least moderately addicted. Caffeine use represents an uncontrolled variable in qEEG and EEG assessment and neurofeedback training. Based

on this review, I believe it is important to inquire as routinely about the amount of caffeine that is used as we do concerning medications that the person is taking. It is my clinical impression that many of our adult ADD/ADHD patients particularly rely on caffeine to assist them in concentrating. Brain levels of caffeine remain stable for at least an hour after intake and it has a half-life of 3 to 8 hours (Axelrod & Reisenthal, 1953; Rowland & Tozer, 1980). Thus, it is my recommendation that whenever possible we should request that patients do not use caffeine in the 4 to 6 hours prior to gathering qEEG or EEG evaluation data. However, we are also walking a tight rope, because to avoid the increase in theta and delta, and the decreases in beta along with withdrawal symptoms such as headache and drowsiness which can negatively affect obtaining reliable data, we should probably discourage caffeine use for no longer than 8 to 10 hours prior to evaluation. The reasoning here is that research finds that withdrawal symptoms typically begin 12 to 24 hours after cessation of caffeine intake (Griffiths & Mumford, 1995). Therefore, if regular caffeine users have not had caffeine since the middle of the afternoon on the day prior to a qEEG evaluation, we certainly should not deprive them of morning coffee or we risk withdrawal symptoms. In conducting neurofeedback training, I believe that we are also wise to make inquiries about the extent of and timing of caffeine use.

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