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Review

Stimulant drugs and vigilance performance: a review

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Abstract. The literature on the effects of some stimulant drugs (amphetamine, methylphenidate, caffeine, and nicotine) on vigilance performance is reviewed. Improvement of overall level of performance (both accuracy and speed) after the intake of amphetamine, caffeine, and nicotine has often been reported, and the decrement in performance with time has been shown to be prevented especially with amphetamine and nicotine. Effects on false alarms are negligible. In studies where a test battery was employed, vigilance tasks appeared to be the most sensitive performance tests in detecting the effects of stimulants; however, different vigilance tasks may measure different aspects of mental functions. There is no support for earlier conclusions that improvements are noticed only in fatigued subjects in protracted sessions. Evidence from several studies does not support the hypothesis that improvements are only a recovery of withdrawal-induced impairment. Because positive effects have been obtained with drugs possessing different mechanisms of action, there is as yet no clear support for a noradrenergic, dopaminergic, or cholinergic theory of sustained attention. Simple neurotransmitter theories of attention and information processing may be untenable.

Key words: Stimulants – Amphetamine – Methylphenidate – Caffeine – Nicotine – Neurotransmitters – Vigilance performance

A large number of experiments investigating the effect of drugs on human performance have been carried out; yet, the subject is usually of minor importance in books on performance and attention or is missing altogether. Neither has the field of psychopharmacology received much recognition in psychological textbooks, although effects of drugs on human behavior have been studied for over 100 years. This is the more surprising because some drugs, notably stimulant drugs, may play a very important role in operational task performance. Nicotine and caffeine, in the form of coffee, tea, or cola drinks, are used every day by millions of people and have been since ancient times: the chewing of plants containing stimulants (for example, ephedrine) dates back to several thousand years B.C. People do so because, besides inducing euphoria, the stimulants are considered to be able to reduce fatigue and to enhance concentration, e.g. in performing protracted, sometimes boring, tasks requiring maintenance of attention in (often) monotonous situations. The principal aim of the present study is to assess whether stimulant drugs really improve impaired performance.

To that end, one particular type of task will be examined in detail, namely vigilance or monitoring tasks. In an earlier review (Koelega 1989) the position has been defended that we may gain more by exhaustive reviews of specific tasks than by reviewing the effects of drugs on "performance" in general. In vigilance tasks people are required to sustain a high level of attention in order to detect aperiodically occurring, rare, or unusual events. In the laboratory, vigilance task performance often shows a decline with the passage of time and the question is whether the deterioration in accuracy and/or speed of performance can be prevented by the use of stimulants. One could argue about the operational relevance of laboratory vigilance tasks, whether they are adequate models of real life situations requiring sustained attention, and about the question of whether "attention", "arousal", "effort", "capacity", or the "allocation of resources" is involved in the performance decrement with time-on-task. These issues will be left undiscussed in the context of the present review, but are addressed in another contribution (Koelega 1993). It is generally agreed that vigilance performance reflects the extent to which, in monotonous situations, a task set can be maintained and distractions can be resisted, which is only one of the components of "attention". There is evidence that laboratory vigilance tasks are experienced as highly stressful and are associated with a high degree of perceived workload.

The first studies on the effects of the stimulant drug caffeine on behavior were carried out in Wilhelm

Wundt's laboratory during the 1880s, and studies on the effects of amphetamine (benzedrine) started some 60 years ago. Early studies of human performance under the influence of amphetamines and caffeine have been reviewed by Weiss and Laties (1962), a "classic", widely cited, review. Weiss and Laties concluded (p 16) that amphetamine can sustain a high level of proficiency, can restore performance that has deteriorated, and contributes something above and beyond what can be achieved with good human engineering design and high motivation. So, an *absolute* improvement in performance is observed, rather than a *relative* improvement (a reduction or prevention of the decrement). It should be noted, however, that their conclusions with respect to vigilance were mainly based on the results of a series of studies by Hauty and Payne (1955) and Payne and Hauty (1954, 1955) with a multidimensional pursuit task, where monitoring (vigilance) was only a component, and the subjects also had to make appropriate movements with joy sticks, pedals, and levers, concurrently. Weiss and Laties (p 30) also dealt with the question of whether superior performance rather than restoring degraded performance is produced by an increase in *capacity* or by making subjects more interested in the task, by inducing favorable attitudes and enhanced *motivation*. Their conclusion was that there are strong indications that the amphetamines, and perhaps caffeine as well, can do *more* than merely restore performance degraded by factors such as boredom, sleep deprivation, and fatigue. However, in a more recent review, Spiegel (1978) concluded that improved performance with stimulants only occurs in fatigued and sleep-deprived subjects, a conclusion also reached by Dews (1984) with respect to caffeine. More recently, Bruce et al. (1986) and Fagan et al. (1988) have also suggested that the effects of caffeine can only be detected in tests of long duration (at least 1 h). We shall examine whether the evidence supports one position or the other.

Apart from amphetamine and caffeine studies, experiments using methylphenidate and nicotine will also be reviewed. The four drugs have a different mechanism of action. Amphetamine and methylphenidate mimic the actions of the catecholamines, mainly noradrenaline (NA) and dopamine (DA), caffeine blocks the receptors for the neuromodulator adenosine, which modifies neurotransmitter release, and nicotine's mechanism of action is mainly cholinergic; nicotine is classified here as a stimulant drug but it has a biphasic action, also possessing depressant (de-arousing) phases of action (see Warburton and Wesnes 1978). In the literature several hypotheses with respect to the neurotransmitter substrate of vigilance have been proposed. Tucker and Williamson (1984), drawing on the classification of neural systems involved in attention provided by Pribram and McGuinness (1975), favor a left-lateralized dopaminergic view of vigilant readiness, Posner and Petersen (1990) propose a right-prefrontal noradrenergic mechanism of vigilance, and Warburton and Wesnes (for example, 1984) have advanced a cholinergic theory of attention and information processing.

Some biological theories of neuropsychiatric disorders have evolved from the neurochemical mode of action of drugs, for example, the "dopamine theory of schizophrenia", and the "catecholamine theory of depression". If the present review showed improved performance with nicotine but not with amphetamine, or vice versa, we might get some clue with respect to the neurotransmitter(s) involved in sustained attention.

The aim of the present review is to consider only vigilance-type tasks. A disadvantage of this approach is that some aspects of the actions of stimulants cannot be sensibly assessed, for example, consideration of the global or specific effects of these drugs. No attempt will be made to review the effects of stimulants on a broad range of abilities, but an interesting compromise could be the assessment of comparative sensitivity, i.e. the comparison of vigilance tasks with psychomotor, cognitive, and memory measures, in those studies which have included a test battery, a broad range of performance tasks.

Summarizing, the aims of this review are to assess 1) whether stimulant drugs restore deteriorated vigilance performance, both with respect to overall (absolute) level of performance and the decline with time; 2) whether performance is only restored in fatigued or sleep-deprived subjects in long lasting sessions, as proposed by several authors; 3) how the sensitivity of vigilance tasks compares with other performance measures; and 4) whether the evidence supports a particular view with respect to specific neurotransmitters involved in vigilance.

Materials and methods

The way of searching the literature, the ordering of the studies, the inclusion of particular test characteristics purportedly affecting study outcomes, the measures of performance considered etc., are in essence the same as described in an earlier review of the effects of benzodiazepines (Koelega 1989).

No attempt has been made to use meta-analysis in integrating research findings from independent studies. The question of whether stimulants affect vigilance can easily be answered without these statistical procedures. Koelega (1992) has recently indicated some conditions under which a meta-analysis makes sense, and has also addressed the issue of whether all available empirical studies should be included in a review, or only flawless ones. Because in vigilance experiments very few investigators have as yet applied appropriate statistics, any choice to leave some experiments out and others not contains some arbitrariness. In most studies using repeated measures designs, the sphericity problem of repeated measures (the heterogeneity of covariances) has not been adequately dealt with, so completely flawless studies are rare. In the experiments of the present review statistical analyses have often been less than adequate, as indicated in the Appendix; for example, testing time-on-task with a Wilcoxon test between the first and last time block, or carrying out an ANOVA on the differences between first and last block. Of course, early studies such as Mackworth's seminal study, carried out some 45 years ago, cannot be blamed for not employing multivariate or corrected-univariate analyses. But often later studies also fail to report on the interaction of Drugs (placebo versus drug) × Period (time-on-task), which is where we are looking for with respect to effects on the decrement.

Studies investigating the effects of stimulant drugs on vigilance performance, are summarized in Table 1. Details of procedures and results are presented in the Appendix. Experiments using amphetamine have rarely been carried out during the last decade, whereas studies employing caffeine and nicotine are practically confined to the last decade which is somewhat surprising for the two

Table 1. Effects of stimulant drugs on vigilance performance

Study	Drug/ dose (mg)	Time after ingestion (min)	Subjects (sex; age)	Cross-over design	Task				Measure of performance	Effect on overall level	Effect on time course	Remarks (see Appendix)
					Duration (min)	Modality	Event rate (min)	Signal probability				
Part 1: Amphetamine												
1) Mackworth (1950)	*dl*-amph./10	60	24(M; NR)	Yes	120	V	60	0.007	Hits RT	Yes Yes	Yes Yes	1
2) Kornetsky et al. (1959)	*d*-amph./ 10 and 15	130	15(M+F; 18–25)	Yes	20	V	60	0.27/0.20	Hits F.a.s[b]	Yes/No No	NR[a] NR	2
3) Townsend & Mirsky (1960)	*d*-amph./ 5 and 15	135	8(5M;3F; 18–22)	Yes	20	V	60	0.27/0.20	Hits F.a.s	No No	NR NR	3
4) Weiner & Ross (1962)	*d*-amph./15	45	32(M; 18–26)	Yes	120	V	–	–	Responses	No	No	4
5) Loeb et al. (1965)	*d*-amph./10	60	24(M+F; 17–28)	Yes	60	A	24	0.02	Hits F.a.s RT d′ β	NR NR No No No	Yes No Yes No Yes	5
6) Mackworth (1965)	*dl*-amph./10	60	56(F; NR)	Yes	60	V	360	0.008	Hits F.a.s d′	NR NR NR	Yes No Yes	6
7) Neal & Pearson (1966)	*d*-amph./5	60	24(16M; 8F;	Yes	64	A	60	0.01	Hits F.a.s	No No	No No	7
			21–62)	Yes	60	A	20	0.01	Hits F.a.s	No No	No No	
8) Talland & Quarton (1966)	methamph./ 15 mg/150 lb, IV	5	18(M; 21–28)	Yes	60	V	55	0.10	Hits F.a.s	Yes/No No	NR NR	8
9) Bye et al. (1973)	*d*-amph./ Exp. I: 2.5,5.0,7.5 Exp. II: 1,2.5	38, 158, and 278	Exp. I: 12 (9M,3F; 21–46) Exp. II: 12 (7M,5F; 21–47)	Yes	60	A	30	0.02	Hits F.a.s d′ β	Yes No No No	No NR NR NR	9
10) O'Hanlon et al. (1978)	*d*-amph./10	60	17(M; 21–30)	Yes	105	V	24	0.03	Hits	Yes	Yes	10
11) Peck et al. (1979)	*d*-amph./ 5 and 10	60 and 240	12(6M,6F; 21–35)	Yes	60	A	30	0.02	Hits F.a.s	Yes No	NR NR	11
12) Rapoport et al. (1980)	*d*-amph./ 0.25/kg and 0.50/kg	abt. 60	31(M; 18–30)	Yes	8	V	100	0.04	Hits F.a.s	Yes No	NR NR	12
13) Hamilton et al. (1983)	*d*-amph./ 5 and 10	60 and 255	12(6M,6F; 20–41)	Yes	60	A	30	0.02	Hits d′ β	Yes/No Yes/No No	NR NR NR	13

Table 1. Continued

Study	Drug/ dose (mg)	Time after ingestion (min)	Subjects (sex; age)	Cross-over design	Task				Measure of performance	Effect on overall level	Effect on time course	Remarks (see Appendix)
					Duration (min)	Modality	Event rate (min)	Signal probability				
Part 2: Methylphenidate												
14) Hink et al. (1978)	methylph./ 10	30	12(M; 19–28)	Yes	70	A	150	0.05	d′ β	No No	No No	14
15) Coons et al. (1981)	methylph./ 20	100	I: 13(M; mean 24)	Yes	6(3x)	V	60	0.13–0.16	Hits F.a.s	No No	NR NR	15
			II: 23(M; mean 20)	Yes	6–8 (4x)	V	50	0.10–0.20	Hits F.a.s	Yes/No No	NR NR	
16) Aman et al. (1984)	methylph./ 0.3/kg	90	12(5M,7F; 22–43)	Yes	7	V	23	0.40	Hits F.a.s RT	No Yes No	NR NR NR	16
17) Strauss et al. (1984)	methylph./ 20	75	22(M; mean 19)	Yes	45	V	40	0.10	Hits F.a.s RT d′	Yes No Yes No	No No Yes Yes	17
Part 3: Caffeine												
18) Baker & Theologus (1972)	caffeine/ 200 and 400	60, 120, and 180	100(M; mean 23)	No	240	V	–	–	RT	Yes	Yes	18
19) Keister & McLaughlin (1972)	caffeine/200	20	60(M,F; NR)	No	48	A	60	0.01	Hits	No	No	19
20) Clubley et al. (1979)	caffeine/75, 100, 150 and 300	45 and 240	24 (10M, 14F; 21–43)	Yes	60	A	30	0.02	Hits	Yes/No	NR	20
21) Rapoport et al. (1981)	caffeine/ 3 and 10/kg	abt. 60	20(M; mean 22)	Yes	8	V	75	0.05	Hits F.a.s	No No	NR No	21
22) Loke & Meliska (1984)	caffeine/ 195 or 325	5	24(12M, 12F; 18–20)	No	90	V	3	0.22	Hits F.a.s RT	No No No	No No No	22
23) Nicholson et al. (1984)	caffeine/300	75	6(F; 19–34)	Yes	45	V	60	0.04	Errors	Yes	NR	23
24) Borland et al. (1986)	caffeine/300	0, 180, and 360	4(M; 20–26)	Yes	10	V	60	NR	Hits F.a.s	Yes No	NR NR	24
				Yes	10	V	60	NR	Hits	Yes	NR	
				Yes	30	V	60	NR	Hits	Yes	NR	
25) Lieberman et al. (1987b)	caffeine/ 32, 64, 128, and 256	50	20(M; 18–47)	Yes	5	V	150	0.04	Hits F.a.s	No No	NR NR	25
				Yes	60	A	30	0.02	Hits F.a.s	Yes No	NR NR	
26) Lieberman et al. (1987a)	caffeine/64	65	20(M; 18–35)	Yes	60	A	30	0.02	Hits F.a.s	Yes No	NR NR	26
27) Fagan et al. (1988)	caffeine/200	I: 90	8(3M,5F; 20–37)	Yes	60	A	30	0.02	Hits F.a.s	Yes No	NR NR	27
		II: 60	10(5M,5F; 18–36)	Yes	60	A	30	0.02	Hits F.a.s	Yes/No No	NR NR	
				Yes	8	V	30	0.17	Errors	No	NR	

28) Swift & Tiplady (1988)	caffeine/200	60, 120, and 180	6(2M,4F; 18–37) 6(3M,3F; 65–75)	Yes	8	V	30	0.17	Errors	Yes/No	NR	28
29) Rogers et al. (1989)	caffeine/300	30, 165, 300, 435, and 570	6(F; 20–32)	Yes	10 26	V V	60 60	NR NR	Hits Hits	Yes Yes	No No	29
30) Smith et al. (1990)	caffeine/3/ kg	30 and 75	32(16M;16 F; NR)	Yes	10	V	100	0.08	Hits F.a.s RT	Yes No Yes	No No No	30
31) Zwijghuizen-Doorenbos et al. (1980)	caffeine/250	90	24(M; 21–36)	No	40	A	NR	NR	Errors RT	Yes Yes	NR NR	31
32) Frewer & Lader (1991)	caffeine/ 250, 500	45 and 165	12(6M,6F; mean 25.1)	Yes	15	V	100	0.08	Hits F.a.s RT	Yes No Yes	No No No	32
					21	V	cont.	–	Hits F.a.s	Yes No	Yes No	
33) Rosenthal et al. (1991)	caffeine/75 or 150	abt. 75 and 315	24(M; 19–35)	No	40	A	NR	NR	Errors RT	No Yes	NR Yes	33
34) Yu et al. (1991)	caffeine/ 250 mg	30, 60, 90, 120, and 180	19(NR; 60–77)	Yes	8	V	30	0.17	Errors	Yes	NR	34
Part 4: Nicotine												
35) Tarrière & Hartemann (1964)	cigarettes (nicotine and CO)	smoking during task	24(M; NR)	Yes	150	V	–	–	Hits	Yes	Yes	35
36) Myrsten et al. (1975)	id.	id.	16(M; 21–29)	Yes	90	V	40	0.008	RT	Yes/No	NR	36
37) Tong et al. (1977)	id.	5	120(M,F; 18–30)	No	60	A	60	0.02	Hits	No	No	37
38) Wesnes & Warburton (1978)	cigarettes/ nicotine tablets	various	various	Yes	various	V/A	various	various	Hits	Yes	NR	38
39) Tong et al. (1980)	cigarettes	smoking during task	32(M; 18–30)	No	72	A	60	0.017	Hits F.a.s	No No	No/Yes No	39
40) Mangan (1982)	cigarettes	10	24(M; 18–24)	Yes	30	A	20	0.05	Hits F.a.s d′	Yes/No Yes/No Yes	No No No	40
41) Wesnes et al. (1983)	nicotine/ 0,1, and 2	ingested 3× during task	36(18M,18 F; NR)	Yes	80	V	cont.	–	P(I) B″	Yes No	Yes No	41
42) Wesnes & Warburton (1983)	cigarettes/ I: 0.28,0.71,1.65	task after smoking	I: 24(M;NR)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No Yes	NR NR NR	42
	II: 0.0,0.6,1.84		II: 12(6M,6F; NR)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No Yes	Yes No Yes	
43) Wesnes & Revell (1984)	nicotine/ 0 and 1.2	5	12(6M,6F; 18–21)	Yes	15	V	100	0.08	Hits F.a.s RT	No No No	No No No	43

Table 1. Continued

Study	Drug/ dose (mg)	Time after ingestion (min)	Subjects (sex; age)	Cross-over design	Task				Measure of performance	Effect on overall level	Effect on time course	Remarks (see Appendix)
					Duration (min)	Modality	Event rate (min)	Signal probability				
44) Wesnes & Warburton (1984a)	nicotine/ 0.0,0.5,1.0, 1.5	5	12(M;NR)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No Yes	Yes No Yes	44
45) Wesnes & Warburton (1984b)	cigarettes/ 0.9,1.3,1.5, 1.7	task after smoking	25(M; NR)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No Yes	Yes No Yes	45
46) Edwards et al. (1985)	cigarettes/ 0.9,1.5	task after smoking	19(M; 19–22)	Yes	20	V	100	0.08	Hits F.a.s RT	No/Yes No No/Yes	No No Yes	46
47) Revell (1988)	cigarettes/ 1.2,1.5	task during smoking	30(15M,15 F; 18–21)	Yes	20	V	100	0.08	Hits RT	Yes Yes	Yes Yes	47
48) Hughes et al. (1989)	cigarettes	task after smoking	16(M;NR)	No	45	V	30	0.29	RT F.a.s	No Yes	No No	48
49) Parrott & Winder (1989)	cigarettes + nicotine gum/ 2 and 4	task during smoking/ chewing	16(M; 18–26)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No Yes	NR NR NR	49
50) Petrie & Deary (1989)	cigarettes	task after smoking	12(6M,6F; 18–23)	Yes	10	V	100	0.08	Hits F.a.s RT	No No Yes	NR NR NR	50
51) Sahakian et al. (1989)	nicotine/ 0.0,0.4,0.6 0.8 intram.	task after injection	7 (3M,4F; mean 27) 7(6M,1F; mean 70) 7(3M,4F; mean 71)	Yes	7	V	100	0.08	Hits F.a.s RT A′	Yes No Yes Yes	NR NR NR NR	51
52) Jones et al. (1992)	nicotine/ 0.0,0.4,0.6, 0.8 intram.	task after injection	24(12M,12 F; NR) 24(12M,12 F; NR) 22(11M,11 F; NR)	Yes	7	V	100	0.08	Hits F.a.s RT A′ B″	Yes No No Yes No	NR NR NR NR NR	52
53) Parrott & Craig (1992)	cigarettes + nicotine gum/ 0.0, 2 and 4	task during smoking/ 10 min after gum	16(14M,2F; 18–29)	Yes	20	V	100	0.08	Hits F.a.s RT	Yes No No	NR NR NR	53
54) Pritchard et al. (1992)	cigarettes	task after smoking	24(13M, 11F; 18–43)	Yes	20	V	38	0.19	Errors RT	No Yes	NR NR	54

[a] = not reported
[b] = false alarms

most widely and longest used drugs in the world. Further, there are dozens of studies investigating the effect of methylphenidate in attention-deficit children, but very few studies have been carried out with normal adults. There are practically no studies using pemoline, although positive effects on performance were already reported some 25 years ago (Haward 1965; Talland 1966). Recently, two studies (Tiplady et al. 1990; Yu et al. 1991) have reported significant effects of theophylline on vigilance tasks, although caffeine appeared to be the more potent CNS stimulant of the two methylxanthine compounds (Yu et al. 1991); Bartel et al. (1992) failed to find an effect on another type of vigilance task. Because so few experiments are available, pemoline and theophylline have not been included in a special category in Table 1.

For various reasons some studies have been left out. An early study of Solandt and Partridge (1946), often cited as a seminal study on the effects of amphetamine on vigilance, was excluded, because this was in fact an experiment on thresholds of pitch discrimination using just notable differences. A number of studies from Bättig's institute have not been included in the table (Bättig and Buzzi 1986; Michel et al. 1987, 1988; Nil et al. 1988; Hasenfratz et al. 1989a, b, 1991; Michel and Bättig 1989). These authors modified the task often used by Wesnes and Warburton (for example, 1983), the so-called rapid information processing task (which is in fact a version of the 30-year-old Bakan vigilance task but now with a presentation rate of 100/min rather than 60/min). The Swiss modification by Bättig involves presenting the digits at a subject-paced rate rather than at a fixed rate, achieved by increasing the ISI after each error and decreasing it after a hit; performance is assessed in terms of the subject's processing rate (the intervals serving as an inverse measure of performance) rather than in terms of hits, etc. The authors (e.g. Hasenfratz et al. 1989a) claim that this task has advantages over the Wesnes and Warburton version, but the subject-paced character and especially the different measures of performance preclude comparison with the usual type of vigilance task, and for this reason these studies would require a separate table (in contrast to studies 12, 21, and 25 from Table 1 which also employed an adaptive-rate task, but expressed performance in terms of hits, false alarms etc.). The results obtained with the task used by the Swiss investigators sometimes fail to show improvements after smoking or chewing nicotine gum, or the effects are very modest (there was a positive effect of caffeine; Bättig and Buzzi 1986). An interesting finding was that smoking after alcohol diminished the performance decline due to alcohol, albeit not for RT (Michel and Bättig 1989); further, postlunch smoking and coffee failed to affect performance (Hasenfratz et al. 1989b, 1991), and where both caffeine and nicotine alone improved performance, these effects were not additive (Hasenfratz et al. 1991).

Likewise, experiments reported by Keenan et al. (1989) and Hatsukami et al. (1989) were left out of consideration due to the extremely high signal probability used in the task (0.77); these authors used the task described by Yellin (1980), developed to measure the ability to inhibit responses to frequently occurring signals. Some other interesting studies have been left out, in which vigilance was only a minor *component* of task performance, e.g. the experiment by Regina et al. (1974), evaluating the effects of caffeine on alertness in an automobile-driving simulator (caffeine enhanced performance on two measures of alertness related to vigilance, i.e. the number of missed high-beam signals and RT to these signals). Heimstra et al. (1967) investigated the effect of smoking upon performance in an uninterrupted 6-h simulated driving task; two of the measures were vigilance indices (detection of the deflection of a needle, and detection of an increase in the brightness of two red lights); in the first task, non-smokers showed a decrement and smokers did not, and in the second task, deprived smokers made more errors than smokers or non-smokers. An 80-min visual reaction time (responding to an irregularly presented light without warning signal) experiment reported by Frankenhaeuser et al. (1971) was not included: smoking prevented the decrement occurring in the control condition. Finally, an experiment carried out by Kožená et al. (1986) was excluded because sufficient information on task and procedure was not provided.

Results

Inspection of Table 1 shows that *amphetamine* has been reported to improve *overall level* of detection (hits) in 5 studies out of 12, and an additional 3 studies reported improvement under certain conditions (e.g. after an extra dose and sleep loss, in a second session carried out some weeks later, and when several sessions were combined; details are to be found in the Appendix). In four out of six experiments that reported results on the time course, amphetamine prevented a *decrement* in hits. There were no effects on false alarms. Very few studies reported on RT, d′ and beta; generally, no effects were noted on these measures. The effects reported for very low doses (1 mg) in study 9 (sometimes only for quarters of sessions) are noteworthy, although the same research group could not replicate this result using the same task in later experiments (studies 11 and 13). Only one study (O'Hanlon et al. 1978) provided a separate analysis for "decrementers" and "nondecrementers", arguing that when there is no averaged decrement under the placebo condition, one cannot expect that amphetamine will prevent a decline; indeed, amphetamine arrested the deterioration of the decrementing subgroup. The presence of placebo-nondecrementers may obscure time effects of amphetamine in the overall analysis.

There are only four studies reporting on the effects of *methylphenidate* in normal adults. The results on *overall level* are not consistent, not even with the same research group (studies 15 and 17) using identical tasks. The lack of effect was explained in terms of a ceiling effect, the tasks were very easy. Two studies reported on the *decrement:* Hink et al. (1978) reported no effect of methylphenidate on d′, but this is not surprising. There was no decrement in the placebo condition, and the authors used a task in which the vigil was interrupted every 5 min. Strauss et al. (1984) found a significant Drugs × Period interaction for d′. Methylphenidate prevented the decline in sensitivity; for hits, this interaction approached significance.

For *caffeine,* 17 comparisons for *overall level* of hits are available besides an additional 6 for the hybrid measure "errors", i.e. misses plus false alarms. Six comparisons showed no improvement after caffeine, three only under special circumstances (only in a first experiment, only in the second part of a 60-min task, and only with elderly subjects 3 h post-treatment, respectively), and 14 comparisons showed an improvement in hits or errors with the drug. Of the studies reporting no effect, two employed an adaptive-rate task (studies 21 and 25). In study 25, an effect on a second, externally paced, vigilance task was noted with a very low dose of caffeine (32 mg). Interesting are the effects reported in studies 23, 24 and 29 where performance was measured overnight, and in study 31 where the caffeine group also performed better when caffeine was supposed to have already been eliminated from the system. Seven comparisons are available reporting on the *decrement* in hits: only one (study 32) reported an effect of caffeine on the time course in a Continuous Clock task (not in another task), ameliorating with 250 mg but aggravating with 500 mg.

For *nicotine,* 17 comparisons are presented in Table 1 for hits, 11 of which show improvement of *overall level* as an effect of the drug, and 2 others showed improvement under special conditions (only in a "low" nicotine group, and only during the first 10 min of a 20-min task, respectively). Of the 11 improvements, 9 have been obtained with a type of task developed by Wesnes and Warburton (e.g. 1983, 1984a, b), a modification of the Bakan task (detection of sequences of three consecutive odd or even digits), called a "rapid visual information processing" (RVIP) task by the authors. In most cases where detectability improved, speed (RT or response latency) improved also, exceptions being studies 52 and 53. In only two experiments (Wesnes and Revell 1984; Petrie and Deary 1989) was no positive effect on hits found with this task, but the latter study found improved RT. In five out of seven cases, using the same task, the *decrement* was prevented. In order not to complicate things too much, study 38 (by Wesnes and Warburton) has been presented in Table 1 as one experiment, where in fact a number of different experiments had been carried out. Likewise, an experiment has sometimes been presented in Table 1 as producing a positive effect of nicotine although this effect was limited to a particular dose or time period after smoking or intake of nicotine tablets. All these facts are to be found in the Appendix.

Finally, vigilance tasks are compared with other tasks where test batteries were used. Ten studies employing such a battery have investigated the effects of *caffeine* (nos 20, 23, 24, 25, 26, 27, 28, 29, 32, 34). In all ten studies vigilance tasks appeared to be sensitive to the stimulant effect. No other task showed this level of consistency: simple RT (sensitive in 2 out of 3 studies), choice RT (2 out of 5), tapping (3 out of 5), DSST (3 out of 6), STM (0 out of 2), letter cancellation (0 out of 3), CFF (1 out of 4), digit span (0 out of 2). Only three studies (9, 11, 13) used a battery with *amphetamine.* In all three cases the (auditory, Wilkinson) vigilance task showed a significant effect, in contrast to the other measures (simple RT: 1 out of 2; tapping: 1 out of 3; STM, arithmetic, and STM: 0 out of 1). Four studies assessed the effects of *nicotine* with a battery (50, 51, 52, 53). Measures of the RVIP showed sensitivity in all four studies; cf CFF (2 out of 2, however, study 51 was a subsample of 52). All other measures (DSST, STM, digit span, tapping, letter cancellation, Stroop test, inspection time), being employed once, were insensitive, but it should be noted that a particular aspect of letter cancellation (response time, study 53) showed sensitivity as did tapping in a particular subgroup (only in aged subjects, study 52). So, vigilance tasks appear to be the most sensitive objective performance tasks to monitor the effects of stimulant drugs.

In conclusion, although statistical analyses have often been less than adequate, for all four stimulants improvements in overall level of detection have been reported, and especially for amphetamine and nicotine it has been reported that the decrement occurring in the placebo condition was prevented. There were practically no effects of the drugs on false alarms. Vigilance tasks appear to be the most sensitive tasks in test batteries. Since improved performance is also noted in sessions with a duration of 10 min or less (for example, studies 12, 24, 29, 30, 34, 51 and 52, but note that study 52 is the full sample of study 51), there is no support for earlier conclusions that effects are noticed only in fatigued subjects in protracted sessions. However, effects may more easily become manifest under these circumstances: in studies 23, 24 and 29 caffeine had a beneficial effect on many measures of performance during an overnight period of work, from the afternoon until the next morning.

Discussion

The results obtained with some stimulant drugs are rather clear-cut, which in itself is somewhat surprising, since it has been suggested (Fagan et al. 1988) that *stimulation* may be inherently more difficult to detect than *sedation,* either because normal subjects under normal conditions are working fairly close to their optimum performance (ceiling effects) and thus have less room for improvement than for impairment, or because stimulants are less global in their effects than sedative drugs. The majority of reports in the literature are of sedation, with associated impairments. The point raised by Fagan et al., that the effects of sedatives are more global, may be valid. Bruce et al. (1986) have reported that none of their tests (DSST, tapping, RT, cancellation), ..."well-established tests, with known sensitivity to the depressant effects of a wide range of drugs"..., showed effects of caffeine. However, from Table 1 it appears that there are numerous vigilance studies reporting improvements of overall level of performance after the intake of amphetamine, caffeine, and nicotine (for methylphenidate the improvement is less clear but very few studies using this drug are available), and the vigilance decrement occurring under normal conditions has been reported to be prevented especially by amphetamine and nicotine. In some cases it has been reported that nicotine (or smoking) produces *absolute* improvements in performance, above and beyond baseline levels (e.g. Wesnes and Warburton 1983). There are no reports of impaired performance after the intake of stimulants.

It was stated in the Methods section that statistical analyses have not always been adequate. Experiments using repeated measures designs (the within-subjects factor "time-on-task") may have a problem of heterogeneity of correlations among the repeated measures, resulting in an increased likelihood of a Type I error. This problem can be overcome by using univariate ANOVA with planned contrasts (unfortunately, it can never be established whether planned comparisons are not planned post hoc), corrections, or multivariate analysis. The possible presence of positive bias is less important with respect to the F test for main effect of, or interactions with, time-on-task, than for the specific comparisons that typically follow and clarify significant overall F tests (pairwise contrasts). These subcomparisons are very vulnerable to inflated Type I error rates that may reach 10–15 times the nominal alpha when the validity assumptions are violated. I have dwelt at length on this problem with vigilance tasks in a recent meta-analysis (Koelega 1992).

Older studies in particular err on this aspect and there may also be other problems with some experiments, as stated by Morris and Gale (1988). These authors claim to have reviewed all (15) studies on smoking and vigilance, and they conclude that research findings are equivocal, that all possible outcomes have been achieved. Apart from the fact that the tasks used in the majority of the reviewed studies are *not* vigilance tasks, I share these authors' concern with respect to sources of error, but I do not agree with their conclusion that research findings are equivocal and the implicit suggestion that most studies may not be worthy of further consideration.

In Table 1 we can examine whether the studies reporting no effect of the stimulants (it is possible that some of these studies show a nonsignificant trend in the same direction) differ in a systematic way from those reporting improvement with respect to particular parameters, for example, time after intake, length of the session, modality, event rate etc. It is striking that many studies reporting no effect (caffeine nos 19, 22, 33; nicotine nos 37, 39, 48) did not use a crossover design. Further, there is a suggestion (studies 21 and 25) that the so-called adaptive-rate task is a less sensitive instrument that externally paced tasks (see comments on paced versus unpaced tasks in Koelega 1989). It is not evident that the load imposed by the very high event rate of the RVIP task is a critical determinant, there are also positive effects with lower event rates (studies 25, 26, 27) albeit for caffeine; there are very few nicotine studies employing low event rates. Finally, it remains unclear why caffeine often results in higher overall level of performance but not in prevention of the decline with time.

The conclusion that vigilance tasks rank highest in sensitivity to stimulant drug effects was also reached earlier (Koelega 1989) with respect to the effects of (sedative) benzodiazepines, albeit hedged by the finding that in patients, effects were less often noted than in young volunteers. Lieberman et al. (1987b) reported that as little as 32 mg caffeine, typical of the dose found in a single serving of cola beverage, and less than that found in a single cup of coffee, significantly improved auditory vigilance. Some caveats regarding the sensitivity of vigilance tasks must be entered, however. Different vigilance tasks impose different demands upon perceptual discrimination and working memory (Koelega et al. 1989), cf the processing demands of the Mackworth continuous clock (detection of a pause in a moving hand), the Bakan type of task (detection of sequences of odd or even digits), the CPT–X (detection of the letter X) with highly degraded visual stimuli, or the Wilkinson auditory task (detection of a difference in the duration of tones), etc. These tasks contain important differences, and their intercorrelations are often low. Some tasks, labelled as "vigilance tasks", may be rather insensitive. Further, there is confusion because some tasks are termed in a similar way but are in fact quite different, for example, Jarvik et al. (1989) used an "auditory vigilance task" (subjects recorded numbers for 5 min and had to indicate whether they came from the right or left channel circling every fifth number), which differs completely from the 60-min Wilkinson "auditory vigilance task". Likewise, the CAT (Continuous Attention Test) described by Tiplady (1992a) differs considerably from the CAT used by Frewer and Lader (1991).

Tasks should be analysed in detail and tables with detailed data on various versions of vigilance tasks and their sensitivity, as presented in this review and in Koelega (1989), may contribute to information on utility and quality and thus to decisions to use a particular test. Above all, vigilance tasks claim to measure (the waning of) attention. This claim may be questioned in some tasks, for example, tasks in which the subject is bombarded with degraded, barely discriminable stimuli. The nature of a task must be considered if changes due to drugs are to be interpreted in terms of "attention" rather than in terms of perceptual ability, memory, or information-processing speed. According to Tiplady (1992a), performance on the CAT is a valid measure of the ability to sustain attention, not limited by memory capacity or processing speed. But drugs may affect many aspects of abilities, and test batteries should address a broader range of functioning than merely "attention" in order to obtain a profile of a drug's effect. Parrott (1991a, b, c) has recently discussed issues of standardization, validation, and reliability of test batteries and has pointed out that most batteries used in psychopharmacology comprise an ad hoc collection of unstandardized and poorly documented procedure (see also Tiplady 1992b). Good tests (sensitive/reliable/interpretable) should become more widely used, while poorer tests should fall into disuse. In my opinion, some types of vigilance task (for example, versions of the clock test, the RVIP task, the Wilkinson task, and an extended CAT) are good tests, whereas, for example, the DSST is a poorer test because it couples low sensitivity with uncertainty what the test is supposed to measure (at least half a dozen different mental functions may be affected by drugs). Admittedly, one has to bear in mind that not every vigilance task measures the same aspect of attention and processing.

An important point raised in the literature concerns the often heard criticism that "improvements" with stimulants are only a recovery of withdrawal-induced impairment. The argument is never heard in the case of amphetamine, because normal volunteers, rather than amphetamine addicts, were used in these experiments. But the criticism may be valid where caffeine and nicotine are concerned. The argument cannot easily be settled with respect to caffeine: there are practically no human adults who do not use caffeine in one form or another (tea, coffee, cocoa, cola drinks). All that can be said is that in some studies there were no differences between low consumers (less than 60 mg/day, which is less than one cup of coffee) and high consumers (more than 300 mg/day), both groups showing improved vigilance (studies 25 and 26). It does not seem to be unreasonable to expect the high-consuming group to be more deprived. Apart from the studies in Table 1, several other experiments, in which no vigilance tasks were used, failed to find differences on performance between caffeine-deprived and -nondeprived subjects (Kuznicki and Turner 1986; Ratliff-Crain et al. 1989).

Somewhat more can be said with respect to nicotine.

In the recent "Nicotine Issue" of *Psychopharmacology* (vol. 108, no. 4, 1992), Warburton (1992a) addressed this issue and referred to some studies in the issue that challenged the withdrawal-deficit hypothesis (for example, Pritchard et al. 1992). Wesnes and Warburton (1978) had earlier shown that *non*-smokers also improved with nicotine tablets; the authors produced three pieces of evidence that their subjects were not merely restoring deprivation-induced impaired performance to normal levels.

But there is more evidence, to be found in Table 1. The "relief-of-deprivation hypothesis" implies that 1) deprived smokers perform worse than smokers smoking and non-smokers, 2) smokers smoking and non-smokers will not differ, and 3) if the effects on smokers smoking are not really genuine effects above and beyond deprivation-induced impairment, non-smokers' performance will not be improved by nicotine. Tarrière and Hartemann (1964) found no difference between the performance of deprived smokers and non-smokers, but both groups performed worse than smokers smoking. In two studies (Tong et al. 1977, 1980) there was no difference between deprived smokers and smokers smoking. Wesnes et al. (1983) reported that both smokers and non-smokers improved after nicotine, there was no nicotine × smokers/non-smokers interaction. Wesnes and Warburton (1984a) noted that non-smokers improved during the first 10 min of the task with the highest dose of nicotine. Hughes et al. (1989) reported that tobacco withdrawal did not increase the impairment in response speed, and Jones et al. (1992) found a significant improvement of detection, but no difference between smokers and non-smokers.

All this is not to say that the withdrawal-deficit argument has definitively been rendered invalid (both Hatsukami et al. 1989 and Keenan et al. 1989, have reported adverse effects on RT, but not on hits, after 24 h of cigarette deprivation), but there are many pieces of evidence not supporting this argument. Two more recent contributions (abstracts and therefore not included in the table) present conflicting evidence: Knott and Griffiths (1992) showed that deprived smokers had slower RTs and longer P3 latencies of the event-related potential (ERP), but there was no effect on accuracy. However, Halliday et al. (1992), using a different task, reported that nicotine given to *non*-smokers speeded RTs and produced shorter P3 latencies in a difficult task condition, but here also there was no effect on accuracy. It may or may not be coincidental that in all these studies speed but not accuracy was affected (cf Snyder and Henningfield 1989, who also reported an effect of deprivation on speed only, in their performance battery).

The data from Table 1 cannot be used to decide which neurotransmitter is most prominent in attention and information processing in vigilance tasks. Both benzodiazepines (BZs) and alcohol (acting on GABA) reduce performance and several stimulants enhance detections: amphetamine and methylphenidate (mainly dopaminergic, but also noradrenergic actions), caffeine (inhibiting adenosine), and nicotine (mainly cholinergic). Possibly, all neurotransmitters are involved in attention tasks, and simple neurotransmitter hypotheses of sustained attention may be untenable.

The action of drugs cannot be reduced to effects on a single neurotransmitter system; most drugs have multiple effects and the various transmitters are not acting separately. Adenosine may inhibit the release of DA and NA, and caffeine may therefore increase NA and DA synthesis, but it also influences GABA, ACh, and 5–HT (serotonin); caffeine has been shown to counteract the effects of BZs (but not of alcohol), possibly by blocking adenosine receptors. Amphetamine acts on DA, NA, and 5–HT. Nicotine not only produces cholinergic effects but it can also reduce GABA, and it may facilitate dopaminergic transmission. Short-term exposure to nicotine results in release of ACh, NA, DA, 5–HT, vasopressin, growth hormone, and ACTH. Cigarette smoking may increase the circulating levels of peptides (Benowitz 1988); nicotine can be linked to both opioid and dopamine mechanisms (Stolerman 1987). Interesting in this respect is the negative correlation between cigarette smoking and Parkinson's disease, and the (as yet ignored) prevalence of smoking among schizophrenics; in both groups dopaminergic mechanisms are involved.

The hypothesis could be advanced that all effects of drugs on sustained attention are mediated by GABA: benzodiazepines and alcohol impair performance, and both caffeine and nicotine improve performance. All these drugs apparently act on GABA. Highly interesting is that nicotine intake can antagonize the impairing effects of alcohol: in a subject-paced vigilance task (Michel and Bättig 1989), in selective- and divided-attention tasks (Leigh et al. 1977), in visual discrimination (Tong et al. 1974), in tracking (Kerr et al. 1991), and in choice reaction time (Lyon et al. 1975; Kerr et al. 1991). In real-life situations, alcohol often increases the amount and rate of cigarette smoking. However, this hypothesis does not take into account the role of dopamine (apart from the fact that DA also interacts with GABA, see Timmerman 1992): pemoline (acting more selectively on DA and less on NA than amphetamine) also enhances performance. Further, alcohol also has biochemical and behavioral mechanisms in common with opiates, and nicotine also increases the release of peptides. Chemical transmission in the CNS is modified by a cocktail consisting of peptides, of which there are more than 100, amino acids (GABA, glutamate), and amines (DA, NA, 5–HT, ACh). Continually interacting drug effects typically occur in real life, operational, performance, and deserve more attention from investigators. Nicotine interacts with caffeine: after abstaining from coffee drinking, people smoke more cigarettes (Kozlowski 1976) and smoking increases the clearance of caffeine (Parsons and Neims 1978). Social drugs are frequently taken in combination but very few studies have so far focussed on combined effects on performance, notable exceptions being Hasenfratz et al. (1991), Kerr et al. (1991), and Michel and Bättig (1989).

The point of all this is that proponents of cholinergic models of attention and information processing (for example, Warburton and Wesnes 1984; Callaway et al. 1992; Warburton 1992b) seem to overlook the fact that

intake of amphetamine and caffeine results in effects on behavior (performance) almost indistinguishable from the effects of nicotine. It may be questioned whether vague, catchall, concepts such as "attention", "arousal", "information processing" etc., permitting a great variety of meanings to be associated with them, map onto particular neurotransmitter systems; these concepts are merely (overlapping) semantic abstractions. Nicotine, caffeine, and amphetamine appear to exert similar effects on behavioral measures such as hits and RT. These rather crude measures reflect the final, integrated *output* of information processing. If the drugs appear to have different effects on *aspects* of processing, as manifest in ERPs (for example, nicotine speeding up earlier, stimulus related, processes, and amphetamine affecting later, response-preparation, -selection, or -execution-related, processes, or vice versa), this could constitute evidence that different cognitive and neurochemical mechanisms mediate the processing effects. More studies should be carried out with ERPs and selective noradrenergic, dopaminergic, and cholinergic agonists and antagonists. A promising start has been made by Halliday et al. (1989). Note, however, that the functional significance of the various ERP components is far from clear; for example, RT has been shown to correlate with the amplitudes of several components (Koelega et al. 1992).

In conclusion, the present review has shown that 1) various stimulants improve vigilance performance, both in enhancing overall level of performance and in preventing the decrement with time, 2) the effects on false alarms are negligible, 3) vigilance tasks appear to be the most sensitive tasks in detecting effects of stimulants, 4) improvements are not restricted to fatigued subjects and protracted sessions, and 5) neither do improvements occur only in deprivation-induced impaired subjects. Further, it is suggested that simple neurotransmitter models of attention and information processing may be untenable.

Appendix: remarks on Table 1

1. Both accuracy and speed were improved by amphetamine but accuracy much more than speed. The level of efficiency under the drug was not higher than the normal optimum without amphetamine. The subjects preferred working under the drug condition. Statistics were not provided.
2. The subjects were tested after 44 and 68 h of sleep loss. In the first week placebo's were administered, in the second week 10 mg amphetamine at 44 h plus 15 mg at 68 h. The 10 mg dose did not improve performance on two CPTs (X and A–X), but hits increased (compared with placebo after sleep loss) after the extra 15 mg at 68 h, although performance was *not* returned to the *non*-sleep-deprived control level, established prior to the experiment.
3. Two different CPTs (X and A–X) were used.
4. This study is rather unusual in that the index of vigilance performance was the number of observer responses, i.e. lever depressions which revealed the display to observers; pressing the lever (observer response) caused either a wanted or unwanted stimulus which remained available until detected. Detection performance with respect to signals was perfect, but our concern here is that there was no difference between amphetamine and placebo with respect to this index of vigilance performance.
5. The statistical analysis was inadequate: period effects were tested with a Wilcoxon test between the first and third time block, and differences between drugs and placebo were tested with a Friedman-two-way ANOVA, thus preventing interaction effects from manifesting themselves.
6. The ANOVA was carried out on the differences between the first and sixth 10-min period. Amphetamine reduced the decrement but did not affect the initial level of detection.
7. Two different vigilance tasks were used: a more "cognitive" task (Bakan task) and a more "sensory" one (discrimination of tone duration). There were no effects of age and sex.
8. The task was visual search in a continuously changing display. The effect of methamphetamine manifested itself only in the second test session carried out some weeks later, not in the first session. The authors interpreted this in terms of habituation (familiarity) with the drug and the task, and claimed to have furnished evidence for an absolute improvement of vigilance rather than for a relative effect (a gain from reduced efficiency); there was no decrement in the placebo-condition.
9. The tests were repeated with 2-h intervals (the first session was pre-drug). Significant effects on hits were noted for all doses, even 1.0 mg, although during different sessions and different quarters of sessions (at different times of peak drug action). Most improvement took place about 2–3 h after drug intake. Subjective effects only occurred after the highest dose (7.5 mg), so the vigilance task was capable of detecting changes in performance produced by dosages which fail to produce subjective effects.
10. The effect on the decrement was not significant when all subjects were considered but when "decrementers" (subjects showing a decrement in the placebo condition) were analyzed separately, there was a large (40%) increase in detections after amphetamine.
11. The improvement after amphetamine was significant for the 10 mg condition in both sessions (3 h apart), but not for 5 mg.
12. A group of 15 subjects received the low dose, and another group of 16 subjects received the high dose. The effect on hits was significant for the high-dose group only. The error rate was increased by adapting the ISI (reduction after a hit, and increment after a miss or false alarm).
13. The effects of both doses (5 and 10 mg) on hits were significant when both sessions (separated by more than 3 h) were combined, but, taken separately, there was only an effect in the second session and this of 10 mg only. The results for d′ are given for the second

session only: here only 10 mg produced a significant improvement.

14. Subjects performed 10 consecutive runs of 5.3 min each; after each run the vigil was interrupted to indicate the ear to be attended (the task contained a selective-attention component). There was no decrement in the placebo-condition.
15. In the first experiment two versions of the CPT were performed: the CPT–X (twice) and the CPT–BX; each of the three tasks lasted 6 min. In the second experiment the CPT–X and CPT–BX were given once and, in addition, the more difficult CPT-Double (twice). Signal probabilities were somewhat different in all these tasks, ranging from 0.10 to 0.20. Methylphenidate improved the hit score in the second experiment only, for the BX and Double versions. The authors suggested that the lack of a drug effect in the other tasks was due to a floor effect, there were very few misses.
16. There were significantly fewer false alarms under methylphenidate than under the placebo condition. The authors explained the lack of effect on hits in terms of a ceiling effect; the task was very easy.
17. The attenuation of the decrement in hits approached significance. The task was the most difficult version of the CPT, the CPT-Double.
18. The task involved monitoring two red lights that moved apart at random intervals (20 times within each hour); there were no nonsignals. The measure of performance was the occurrence of response blockings (responses more than twice the value of the no-drug condition).
19. The authors claimed to have shown that caffeine prevented a decrement with extraverts but not with introverts, an interpretation which I have questioned before (Koelega 1992).
20. Two experiments were carried out with 12 subjects each. In the first experiment, caffeine improved hits for all three doses (75, 150, and 300 mg) both in the first session and in the second session carried out some $3\ ^1/_2$ h later. In the second experiment, with 12 different subjects, caffeine (100 mg) treatment did not differ from placebo, a result which the authors could not explain.
21. The task used was a CPT–AX with adapted rate (speeded up after a correct answer, introducing a subject-paced element). There was no difference between low and high habitual consumers. In the same study normal children showed a positive effect of caffeine on hits.
22. Subjects had to judge changes in the speed of a signal sweeping across a screen. There was a 2-min break halfway during the task. High consumers made fewer hits later in the task, produced more false alarms, and responded faster than low users.
23. The task was of the Bakan type; performance was tested overnight.
24. Three vigilance tasks were used (CPT–X, CPT–AX, and Bakan), besides two tasks with a vigilance component; five performance sessions were carried out overnight; results differed for the first and second night.
25. Two tasks were used: the visual adaptive-rate CPT, and the auditory Wilkinson task (a modified version with equalized difficulty). Detection in the latter task was improved by caffeine at all doses, even the lowest one (32 mg). There were no differences between high and low consumers.
26. The same modified Wilkinson task was used as in 25.
27. In the second experiment the effect of caffeine on hits was significant only in the second 30 min of the Wilkinson task, corresponding with the first part of the task in the first experiment (90–120 min after intake).
28. Caffeine had no effects in young subjects, but in elderly subjects it improved detection (fewer errors), albeit only at 3 h post-treatment.
29. Performance was measured overnight, in 8 sessions of 1.75 h each, from 1700 hours until 1030 hours the next morning. Caffeine, administered at 2315 hours, improved performance on both tasks in the sessions starting at 0200, 0415, and 0630 hours. Performance on two other tasks with a vigilance component (vigilance plus tracking, and complex vigilance, simulating an air defence surveillance task) also improved.
30. Caffeine removed the well-known post-lunch dip (impairment in performance efficiency after lunch) at both 30 and 75 min after ingestion; there was considerable variation in the nature of the meals consumed.
31. In this study, tolerance to the effects of caffeine was also demonstrated, besides a provocative finding (the caffeine group was also better than the placebo group on the day after caffeine intake) which the authors interpreted in terms of a conditioned alerting response. There was no effect on a divided attention task.
32. A Mackworth-type task, the Continuous Clock test, was more sensitive to caffeine-induced changes than a rapid-rate Bakan-type task. In the clock task, 250 mg offset the decrement at both post-drug administration times; the 500 mg dose impaired performance at 45 min and improved it at 165 min.
33. Caffeine improved RT only in the second half of the 40-min task, especially after restricted nocturnal sleep (5 h in bed).
34. Subjects were elderly volunteers. There was no effect of caffeine on another (5-min) visual task, the details of which are not provided.
35. The task involved detection of brief and weak flashes in watching a film simulating driving a car on a road; 8 signals per 30 min were presented, there were no nonsignals. Smokers were allowed to smoke normally during the session and were compared with a condition after abstaining from smoking for 20 h.
36. The study showed an interaction between desire to smoke, characteristics of the individual, and the external environment: "low-arousal smokers" performed better on the vigilance task after smoking but not on a highly complex task, whereas "high-arousal

smokers" showed the reverse pattern. The groups did not differ under non-smoking conditions.

37. The authors interpreted their results in terms of superior performance of non-smokers. However, this was a between-subjects design and the groups clearly differed in baseline value. Moreover, the "smokers smoking" group, which is compared with "smokers not smoking" here, was only allowed to smoke before the session, not during task performance. Smokers smoking improved their performance as the vigil progressed.
38. The authors carried out seven experiments, both with cigarettes and nicotine tablets and with different vigilance tasks (Mackworth Continuous Clock, tone detection, and a rapid-rate Bakan task), controlling for the act of smoking (manipulation of cigarettes).
39. Smoking prevented the vigilance decline when only the first three 12-min blocks (out of six blocks) were considered. As in their 1977 study, the authors used a between-subjects design.
40. Subjects were assigned to either a "low" nicotine group (0.7 mg) or a "middle" nicotine group (1.3 mg) and served as their own control in a non-smoking session. A cigarette was smoked prior to the task. The low group had more hits than control (the high group did not), and the high group had fewer false alarms (the low group showed no difference).
41. The task used was the clock test (detecting a brief pause in the continuous movement of the hand). Nicotine manifested its effect after the second tablet (at 40 min). The effects were independent of the smoking status, i.e. also occurred in non-smokers which argues against "dependence-type" explanations that smoking is simply returning performance back to baseline levels in smokers.
42. Two experiments were carried out; in the first one (without placebo) a dose-dependent effect was found; the second experiment included both a placebo cigarette and a no smoking condition.
43. Only the second experiment is considered here; nicotine counteracted the disruption of performance by scopolamine, but there were no differences between nicotine and placebo, which the authors explained in terms of the long rest period following baseline.
44. The prevention of the declines in detections and speed which occurred in the placebo condition was significant for the highest dose (1.5 mg) only.
45. Higher nicotine yielding cigarettes produced greater improvements than lower yielding cigarettes, although there was no monotonic relationship, from which the authors inferred that there might be an optimal delivery of nicotine. There was a non-smoking control condition.
46. There were no effects of cigarettes compared with non-smoking, for the 20-min task, but smoking improved hits and RT when the first 10 min post-treatment only were considered, confirming that nicotine has short-term effects. There was an associated decrease in ERP–P3 latency.
47. Cigarettes were compared with two control conditions (not-smoking and sham-smoking) with a puff-by-puff analysis: smoking commenced at minute 6 with a puff every minute until minute 15; hits increased from around minute 7, the second puff; speed improved from minute 8 onwards.
48. Smokers were assigned to be deprived for the 24 h prior to the task or to continue to smoke during this period. There were no effects on RT, but RT variability increased in the deprived group; false alarms decreased in the smoking group but remained stable in the deprived group.
49. There were three chewing gum conditions (placebo, 2 mg, 4 mg) and a cigarette smoking condition. Hits increased with smoking, and 4 mg gum, and decreased under placebo, RT was faster under 4 mg. Nicotine had a dose-dependent effect on hits, the peak effects of 4 mg gum were around 50% of the effects of cigarette levels.
50. A minute-by-minute analysis showed that RT improved in the smoking condition only during the first 5 min of the task.
51. There were three groups: young normal, elderly normal, and Alzheimer patients. The normal young group and the Alzheimer group showed a dose-dependent improvement, in hits, sensitivity, and RT. Nicotine did not affect a short-term memory task.
52. This study is the full sample of study 51. The task was individually graded in difficulty. There was an interaction group × drug for RT. No differences were found between smokers and non-smokers.
53. The effect of nicotine gum was intermediate between those of placebo and cigarette smoking. For some conditions there was evidence for a monotonic dose-response relationship.
54. Subjects were non-deprived smokers. The task (a CPT) was atypical in that subjects were also required to respond to nonsignals and received feedback, and there was a pay-off matrix.

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