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Latent Inhibition in Smokers vs. Nonsmokers: Interaction With Number or Intensity of Preexposures?

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DELLA CASA, V., I. HÖFER AND J. FELDON. *Latent inhibition in smokers and nonsmokers: Interaction with number or intensity of preexposures?* PHARMACOL BIOCHEM BEHAV **62**(2) 353–359, 1999.—Latent inhibition (LI) refers to the slowing of learning about a stimulus after preexposure, i.e., previous presentation of the stimulus without any consequence. This report summarizes results of four studies investigating the effect of being a smoker or nonsmoker on auditory LI as a function of procedural parameters, namely number (10 vs. 30) and intensity (low vs. high) of preexposed stimuli. In general, the number of preexposures did not affect LI, whereas low-intensity stimuli led to greater LI than high-intensity stimuli. These findings underline the importance of automatic vs. controlled processing of the preexposed stimuli for the development of human LI. Smokers showed increased LI compared to nonsmokers in low-intensity task versions as well as compared to both smokers and nonsmokers in high-intensity versions. These findings may indicate that nicotinic effects on LI depend on the robustness of LI in the control group. © 1999 Elsevier Science Inc.

Latent inhibition Attention Smoking Nicotine Human

FROM the huge amount of stimuli with which we are confronted at any given time, irrelevant stimuli must be ignored or gated out in order to allow concentration on relevant stimuli. One of the experimental paradigms used to assess the ability to gate out irrelevant stimuli is latent inhibition. Latent inhibition (LI) refers to the retarded learning of an association between a stimulus and an outcome following the preexposure to this stimulus without any consequence. Latent inhibition is considered to reflect a process of learning not to attend to, or to ignore, irrelevant stimuli (18,19). The LI paradigm has been studied first in animals (21) and subsequently also in humans [for a review, see (20)].

The typical human latent inhibition paradigm includes two groups of subjects who complete two task phases. During the first—preexposure—phase, one group of subjects, while solving a masking task, is preexposed to a stimulus (e.g., noise), that will be the target stimulus in the subsequent test phase. The other group is treated identically, i.e., the subjects also solve the masking task, but without preexposure to the target stimulus. In the second—test—phase, all subjects perform a learning task in which the preexposed stimulus predicts a consequence (e.g., an increase of a number on a computer monitor). The subjects are required to detect the relationship between the stimulus and the consequence, with trials to reach the learning criterion as the dependent variable. Typically, the preexposed group (PE) learns more slowly than the nonpreexposed group (NPE), and this difference constitutes LI. For the development of this type of LI (instrumental rule learning paradigm) in human adults, a masking task during preexposure is necessary to divert subjects' attention from and achieve automatic processing of the preexposed stimuli. Without a masking task, the preexposed stimuli would be processed in a controlled manner, including conscious verbal conjectures about the stimuli and their meaning, thus preventing LI (20).

Animal experiments have provided evidence that LI is abolished by indirect dopamine agonists like amphetamine [e.g., (10,28,30–32) and enhanced by dopamine antagonists like haloperidol [e.g., (10,15,26)]. Similar effects have been re-

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ported from experiments with human subjects [agonists: (13,29), antagonists (33,34)]. Based on the evidence for dopaminergic modulation of LI, nicotine, which also increases the dopaminergic activity in the mesolimbic dopamine system (14), has been hypothesized to lead to reduced LI. In support of this hypothesis, LI has been shown to be reduced in animals after nicotine vs. vehicle administration (12,15,22,23,25), but has also been found to be enhanced [(25), see below]. In humans, LI has been found to be unaffected by acute nicotine (12,29). In contrast, effects of chronic nicotine have been reported, namely reduced LI in smokers as compared with nonsmokers (1).

We recently reported results from two studies on the effects of smoking status on human auditory LI (9). The first study, using 10 stimulus preexposures, revealed similar LI in nonsmokers and three smoker groups, which differed with respect to acute nicotinic state. The failure to find the expected reduced LI in smokers might have been a consequence of a floor effect, as the LI effect in the control subjects (nonsmokers) turned out to be rather weak. The second study, using 30 instead of 10 stimulus preexposures, yielded greater LI in the control subjects. Unexpectedly, the second study provided some evidence that smokers, irrespective of being deprived or not overnight or having smoked or not just before the experimental task, showed greater LI than nonsmokers (logistic regression for dichotomized learning criterion).

We attributed the different results, i.e., no smoking effect after 10 preexposures and enhancement of LI in smokers after 30 preexposures, to differences in total preexposure duration, in line with the interaction between preexposure duration and nicotinic effects on LI reported from animal experiments. Acute nicotine has been found to attenuate LI after short preexposure duration and to enhance LI after long total preexposure duration (25). However, our different results with 10 and 30 preexposures could also have derived from another procedural parameter. In the first study, we used 10 preexposures of high intensity (loudness) stimuli, whereas, in the second study, we used 30 preexposures of low intensity stimuli.

By investigating the two missing conditions, the different effect of smoking status on LI could be attributed unequivocally to number or intensity of preexposures. Accordingly, we conducted two additional studies which used 10 preexposures of low-intensity stimuli or 30 preexposures of high-intensity stimuli, respectively. The previously (9) claimed critical role of number (or total duration) of preexposure would be supported if the new "10 low" study replicated the results of the former "10 high" study, namely no LI difference between nonsmokers and smokers, and the new "30 high" study replicated the results of the former "30 low" study, namely enhanced LI in smokers. For these new studies, nonsmokers and smokers irrespective of acute nicotinic state were considered, because according to the studies reported so far (1,9,12,29) being a smoker or a nonsmoker might affect human LI, whereas acute nicotine administration appears not to affect human LI. The data of our two former studies, which considered smokers in three different nicotinic states, were reanalyzed accordingly, i.e., collapsing over different smoker states to constitute one group of smokers. In an attempt to find out more about stimulus processing during preexposure, preexposed subjects of the two new studies were retrospectively asked for their hypotheses about the meaning of the preexposed stimuli.

Because this series of four experiments is the first to manipulate number and intensity of preexposures according to a complete 2×2 design, the data of all four studies were also submitted to combined analysis. This allows to further elucidate the effects of number and intensity of preexposures on human auditory LI, as well as its interaction with being a nonsmoker or a smoker.

METHOD

Subjects

A total of 379 healthy paid volunteers, 191 females and 188 males, with a mean age of 32 years (range 22 to 46) participated in the four studies. Subjects were selected from responders to advertisements in a local newspaper. Those with a severe medical illness, a history of psychiatric illness, or current treatment with centrally acting medication or drug abuse were excluded. Smokers were required to smoke habitually at least 15 cigarettes per day; subjects who reported not smoking were considered as nonsmokers.

Subjects' demographic characteristics are summarized in Table 1. Smokers and nonsmokers and PE and NPE groups did not differ with respect to demographic variables. Study-specific subsamples differed only in that subjects in the two studies using 10 preexposures had completed 1 year more of

TABLE 1

SUBJECTS' DEMOGRAPHIC CHARACTERISTICS (MEANS AND STANDARD ERRORS)

Sample	*N* (total 379)	Age (Years)	Education (Years)	Cigarettes/ Day†	Nicotine (mg/cig)†	Tar (mg/cig)†
10 Low all	109	32.2 ± 0.5	13.8 ±0. 2			
Smokers	58	32.6 ± 0.6	14.0 ± 0.3	22.5 ± 1.0	0.59 ± 0.03	7.1 ± 0.5
Nonsmokers	51	31.8 ± 0.7	13.6 ± 0.3			
10 High all*	105	31.4 ± 0.5	14.0 ± 0.3			
Smokers	73	31.8 ± 0.7	13.7 ± 0.3	20.7 ± 0.7	0.68 ± 0.02	8.5 ± 0.4
Nonsmokers	32	30.5 ± 0.7	14.7 ± 0.5			
30 Low all*	102	31.9 ± 0.5	13.2 ± 0.2			
Smokers	75	32.0 ± 0.6	13.1 ± 0.2	23.8 ± 1.0	0.65 ± 0.03	7.9 ± 0.4
Nonsmokers	27	31.6 ± 1.0	13.6 ± 0.6			
30 High all	63	30.3 ± 0.6	12.7 ± 0.3			
Smokers	37	29.6 ± 0.8	12.6 ± 0.4	22.0 ± 1.4	0.61 ± 0.05	7.5 ± 0.4
Nonsmokers	26	31.5 ± 1.0	13.0 ± 0.4			

*Della Casa et al., in press.

†Smokers only.

education than subjects in the two studies using 30 preexposures (13.9 ± 0.2 vs. 13.0 ± 0.3; $p < 0.01$).

Auditory Latent Inhibition

The auditory LI test was a computerized version of the auditory LI task originally described by Ginton et al. (11), slightly modified from those described subsequently in the literature (1–3,13,33).

During the first phase, the preexposure phase, all subjects listened through binaural headphones to a tape (AJ Sound and Vision Ltd., UK) with repeated cycles of 40 "nonsense" syllables, spoken in a male voice and presented at approximately 57 dB(A). The interval between syllables was 1–2 s. As a masking task, all subjects had to count the frequency of one of the nonsense syllables ("NIB"). Nonpreexposed (NPE) subjects heard nonsense syllables only, whereas preexposed subjects (PE) listened to the nonsense syllables with superimposed bursts of white noise (duration 1–2.5 s; average interstimulus interval of 10.7 s). The procedural details of the four task versions are listed in Table 2.

The second phase, the test phase, was the same for PE and NPE subjects. It consisted of six binaurally presented cycles of the nonsense syllables, and white noises with an interstimulus interval of 9.8 s. Each white noise caused the increment of a number, starting with 10, displayed in the center of the computer screen. Subjects were required to find out the relationship between something they heard (white noise) and the increment of the number on the screen and to press a button as quickly as possible whenever they thought the number was going to increase. After four consecutive correct responses (without errors of omission and commission) or after 36 white noise–number increment pairings the test was terminated automatically. The number of the first white noise eliciting this quadruplet of correct responses was used as dependent variable (number of trials to learn). Subjects, who did not learn the noise–number increment relationship, were given a score of 36.

Procedure

After initial instructions, subjects gave their written informed consent on a form approved by the Ethical Committee of the Swiss Federal Institute of Technology Zurich. After collection of general information, and screening of subject's hearing (Bosch audiometer ST10, Robert Bosch GmbH, Germany) at 500, 1000 and 6000 Hz and a loudness of 40 dB(A), subjects were seated approximately 75 cm away from the computer screen in an indirectly illuminated, sound-attenuated room. Subjects first completed a visual associative conditioning task to familiarize them with the nature of the subsequent LI task. The screen displayed the number 10 centrally in white and, around the central number, a shape which changed every 1.5s in form (ellipse, rectangle), size, height-to-width ratio, and color. The central number increased in value 1.25 s after the appearance of a rectangle. Subjects were required to find out the relationship between something they saw (rectangle) and the increment of the number. They were asked to press a mouse button when they thought that the number would increase, i.e., during the time interval between the appearance of the stimulus and the actual increment of the number. If a subject did not solve the task, the instructions and the task were repeated. Afterwards, subjects completed a computerized personality questionnaire (4), and some smokers smoked a cigarette. Then, subjects completed the auditory LI task, and afterwards preexposed subjects in the "30 high" and in a part of the "10 low" study were asked for their subjective explanations for the occurrence of the white noises during the preexposure phase as follows: "What exactly did you hear on the tape? What did you think, when you heard the noises? How did you explain the presence of the noises?" Subjects who did not spontaneously report having heard the noises, were explicitly asked whether they could remember the presence of any noise. Finally, subjects were debriefed and paid.

TABLE 2

PROCEDURAL DETAILS OF THE PREEXPOSURE PHASE IN THE FOUR AUDITORY LI TASK VERSIONS

	10 High	10 Low	30 High	30 Low
Number of white noises	10	10	30	30
Total duration of white noises (s)	17.5	17.5	54.0	54.0
Loudness of white noises in dB(A) (preexposure and test phase)	~46	~42	~46	~42
Loudness of syllables in dB(A)	57	57	57	57
Number of syllable cycles	1.5	1.5	5	5
Total duration of preexposure phase (min)	2	2	5	5

Statistics

First, the data of each study were analyzed separately according to a 2 × 2 design (preexposure, i.e., PE vs. NPE; group, i.e., smokers vs. nonsmokers). Thus, the former studies "10 high" and "30 low" were reanalyzed by combining the three smoker groups to a single one and contrasting it with nonsmokers. Second, the combined data of all four studies were analyzed according to a 2 × 2 × 2 × 2 design (intensity of preexposures, i.e., low vs. high; number of preexposures, i.e., 10 vs. 30; preexposure, i.e., PE vs. NPE; group, i.e., smokers vs. nonsmokers).

The LI data were bimodally distributed and censored because the task ended regardless of whether or not the subject had learned. Therefore, number of trials to reach the criterion of four correct responses was analyzed with Cox proportional hazards regression analysis (16,17). The Cox hazard regression analysis tests the effects of independent variables (continuous or categorical) on a usually time-related dependent variable, which is represented as hazard function (survival curve); the method makes no assumptions with respect to the distribution of hazards, except proportionality. The learning criterion in LI tasks can be considered as survival time or hazard (trials until the "risk" to learn); not learning within the maximum number of trials [36] represents censored scores. Cox regression can be used like an analysis of variance (ANOVA), when including as independent variables interactions as well as single variables. To similarly control for lower order effects, main effects (preexposure, group, loudness of preexposure, number of preexposure), two-way, three-way, and four-way interactions were entered into the model in subsequent "blocks," excluding for each block separately all nonsignificant predictors (according to the likelihood ratio method LR). The Cox regression provides Wald-values and corresponding significance levels for the individual effects, which correspond to *F*-values from an ANOVA. The reported Wald-values, with 1 degree of freedom, derive from the final

reduced model. For (significant) effects in the model, the Cox regression provides b-values and their standard errors, which indicate the deviation of the level-specific survival curve from the overall mean survival curve. Statistical analysis was done with the SPSS 6.1 package.

In addition to medians for the NPE/PE groups, we report "mean AUC" values corresponding to the area under the Kaplan-Meier survival curve (for convenience expressed as percentage instead of probability; for comparability across different ranges of the x-axis, i.e., also other studies, divided by number of x-values, here 36).

The self-reported explanations for the white noise during preexposure were coded as "white noise recorded intentionally" or "representing a common disturbance (due to bad recording or old tape)," and analyzed using the Chi-square test.

RESULTS

Study Specific Analysis

As can be seen in Fig. 1a, PE subjects in all four studies reached the learning criterion slower than NPE subjects, indicating LI (cf. also Table 3). Separate analyses for smokers and nonsmokers replicated this finding (Fig. 1b and c, Table 3), with the exception of nonsmokers in the "30 high" study, who failed to show significant LI.

With respect to differences of LI between smokers and nonsmokers, the descriptive statistics (Fig. 1b and c, Table 3) suggest that smokers in the two low intensity studies showed more pronounced LI than nonsmokers due to retarded learning ("prolonged survival") of PE smokers. Cox regression indeed provided evidence for greater LI in smokers than nonsmokers for the "10 low" study (group × preexposure: $b = 0.26 \pm 0.11$, Wald = 5.26, $p < 0.03$). For the "30 low" study, such a difference was less clear (group × preexposure, Cox regression: $b = 0.16 \pm 0.14$, $p > 0.25$), statistical significance was reached only when using logistic regression for the dichotomized learning criterion [(cf. (9); fast vs. slow = within vs. after 10 trials; group × preexposure: $b = 0.76 \pm 0.32$, Wald = 5.74, $p < 0.02$). In the high-intensity studies, however, no evidence for differences in LI between smokers and nonsmokers emerged (group × preexposure: ps > 0.45).

Subjective Data

The subjective explanations for the white noise during preexposure differed significantly between the two task versions [$\chi^2(1) = 6.25$, $p < 0.01$]: in the "30 high" study ($n = 31$), 71% of the preexposed subjects considered the white noise to be recorded intentionally (to distract their attention from the masking task), whereas in the "10 low" study ($n = 35$) this was reported only by 37%. Smokers and nonsmokers did not differ with respect to their subjective explanations ("30 high": 67 vs. 77%, $n = 18, 13$; $p > 0.65$; "10 low": 43 vs. 14%, $n = 28, 7$; $p > 0.20$).

Combined Analysis

To validate the different effects of smokers vs. nonsmokers on LI, and to further elucidate the effects of number and in-

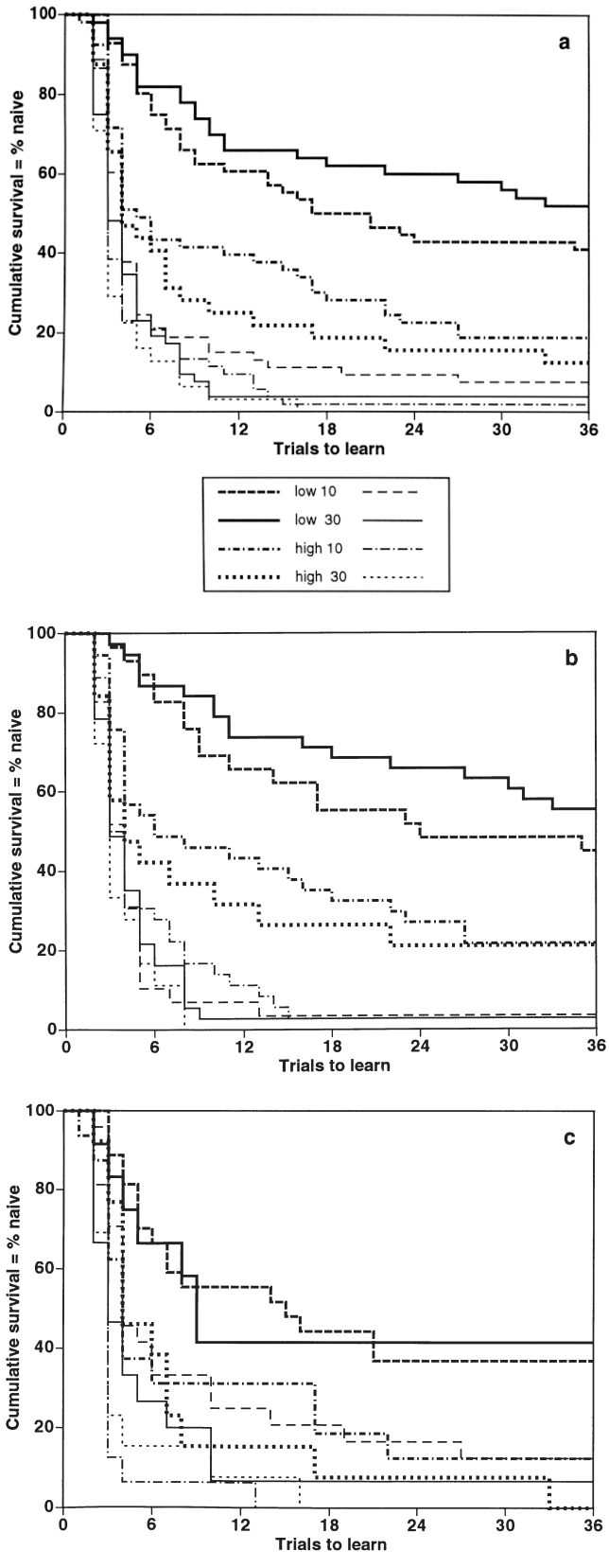

FIG. 1. Cumulative survival curves for auditory LI, split by preexposure (PE—thick lines, NPE—thin lines) and task version (10 low, 30 low, 10 high, 30 high) for: (a) all subjects, (b) smokers, and (c) nonsmokers. The y-axis represents cumulative survival in percent, corresponding to the percentage of subjects who have not learned the stimulus–consequence relationship ("naive").

TABLE 3
SYNOPSIS OF RESULTS IN THE FOUR STUDIES FOR ALL SUBJECTS AND SPLIT BY SMOKERS/NONSMOKERS

	All					Nonsmokers				Smokers			
			Preexposure		Group * Preexp			Preexposure				Preexposure	
Study	Med*	AUC†	b ± SE	*p*	b ± SE‡	*p*	Med*	AUC†	b ± SE‡	*p*	Med*	AUC†	b ± SE	*p*
10 High	3/5	12/35	0.42 ± 0.11	0.00	0.04 ± 0.11	0.74	3/4	7/26	0.42 ± 0.21	0.04	3.5/6	14/38	0.40 ± 0.13	0.01
30 High	3/5	8/26	0.37 ± 0.14	0.01	0.09 ± 0.14	0.49	3/6.5	9/19	0.34 ± 0.21	0.10	3/4.5	8/31	0.40 ± 0.19	0.04
10 Low	4/19	18/57	0.64 ± 0.12	0.00	0.26 ± 0.11	0.02	4/15	26/50	0.38 ± 0.17	0.02	4/24	11/62	0.92 ± 0.18	0.00
30 Low	3/36	12/67	0.90 ± 0.14	0.00	0.16 ± 0.14	0.25	3/9	15/49	0.49 ± 0.24	0.04	3/36	11/72	1.08 ± 0.17	0.00
High							3/4	8/23	0.42 ± 0.15	0.01	11/35	3/3.5	0.40 ± 0.11	0.01
Low							4/14	22/50	0.43 ± 0.13	0.01	11/65	3.5/36	1.00 ± 0.12	0.00

*Median trials to reach criterion for NPE/PE.
†Mean AUC for NPE/PE.
‡Nonsignificant *b*-values derive from the last model before exclusion of the effect.

tensity of preexposures on LI, the data of all studies were submitted to combined Cox analysis. In the whole sample, there was a strong overall LI effect (preexposure: b = 0.54 ± 0.07, Wald = 68.79, $p < 0.01$). Low intensity of the preexposed stimuli yielded stronger LI than high intensity (intensity × preexposure: b = 0.17 ± 0.06, Wald = 8.26, $p < 0.01$), due to slower learning in the low intensity PE groups (see Fig. 1a). In addition, low intensity led to slower learning than high intensity, independently of preexposure condition (intensity: b = 0.32 ± 0.06, Wald = 25.49, $p < 0.01$). The number of preexposures did not affect learning (number: $p > 0.35$) or LI (number × preexposure: $p > 0.25$), nor did the interaction of number and intensity of preexposures (number × intensity, × preexposure: ps > 0.30). Depending on the level of lower order effects that were controlled for, the three-way interaction group × intensity × preexposure was significant ($p = 0.008$) or not ($p = 0.12$). To further clarify this picture, separate analyses for smokers and nonsmokers were conducted.

Although overall LI was revealed in smokers as well as in nonsmokers (preexposure: ps < 0.01), intensity affected LI only in smokers (intensity × preexposure: b = 0.25 ± 0.07, Wald = 10.88, $p < 0.01$), but not in nonsmokers (intensity × preexposure: b = 0.02 ± 0.09, $p > 0.75$). These findings indicate that LI was enhanced in smokers in the low-intensity versions. In addition, the main effect of intensity was obtained for both smokers (intensity: b = 0.23 ± 0.07, Wald = 9.46, $p <$ 0.01) and nonsmokers (intensity: b = 0.39 ± 0.10, Wald = 16.30, $p < 0.01$). Number of preexposures and the interaction of number and intensity of preexposures did not affect learning or LI in smokers or in nonsmokers (number, × preexposure; number × intensity, × preexposure: ps > 0.25).

DISCUSSION

The present report is the first to analyze the influence of intensity and number of preexposures on human auditory LI, and the interaction of these procedural parameters with smoking status. Subjects preexposed to a white noise required more trials to learn the association between this stimulus and a consequence than subjects who were not preexposed. Thus, we obtained significant auditory LI in the combined sample and all subsamples with the exception of nonsmokers in the "30 high" version.

Before discussing the results in detail, several caveats should be mentioned that might limit the interpretation of the results. First, the four different task versions were not investigated in a single experiment (with intermixed random assignment of subjects to the different number and intensity of preexposures conditions), but in subsequent runs. However, the study groups had comparable demographic characteristics, except for years of education (10 vs. 30 preexposures). Second, the significant main effect of intensity, indicating that all subjects, irrespective of being preexposed or not, took longer to solve the learning task in low- than in high-intensity versions, might lead to the suspicion that the low-intensity white noises were more difficult to hear and even missed by some subjects. However, the positive hearing test at 40 dB(A) suggests that all subjects were able to perceive 42 dB(A) white noises, and in fact, the vast majority of NPE subjects solved the learning task. The audibility of the low intensity noises is supported by the fact that all subjects who did not solve the task, when informed about the correct solution and explicitly asked for their perceptions, affirmed having heard the noises. Finally, the detection of smoking effects on LI may have been complicated by the unequal sample sizes of smokers and nonsmokers. Because Cox regression analysis does not control for un-

equal cell sizes, the predictors were correlated, which might have led to an overestimation of lower order effects and a conservative (under-) estimation of higher order effects (interactions).

With respect to smoking effects on LI, the new "10 low" study replicated our former "30 low" result, namely enhanced LI in smokers, and the new "30 high" study replicated our former "10 high" result, namely no effect of smoking on LI. The combined analyses also revealed that LI was enhanced in smokers when using preexposure stimuli of low intensity. Thus, it turns out that intensity of the preexposed stimuli is the critical factor that modulates the effects of smoking on LI and not number or duration of preexposures as formerly hypothesized (9). This explanation had been derived from the fact that duration of preexposure was the experimental variable that modulated the effect of nicotine on LI in the animal studies (25).

Rochford et al. (25) hypothesized robustness of LI in the control group (placebo) to be the critical factor, whereby "labile" control-LI allows for an attenuating effect of nicotine, and "robust" control-LI allows for an enhancing effect of nicotine. In our studies, weaker or labile control-LI (nonsmokers) with high-intensity stimuli yielded no effect of smoking status on LI, while larger or "robust" control-LI with low-intensity stimuli yielded enhanced LI in smokers. Thus, the effects on LI of both acute nicotine in animals and of being a smoker, which might reflect the effects of chronic nicotine in humans, appear to increase with robustness of LI in the control group. In contrast, Allan et al. (1) reported reduced LI in smokers compared with nonsmokers, who showed very robust LI (medians for NPE/PE 4/36, estimated from figure). However, the comparability of our and Allan et al.'s LI results appears to be restricted due to differences in the definition of smokers (15 or more cigarettes per day vs. unselected) and differences in the procedure.

Rochford et al. further hypothesized that the nicotine-induced reduction of LI is mediated via activation of dopaminergic substrates, while the enhancement of LI is mediated through cholinergic substrates by means of two distinct mechanisms, one acting on neurobiological substrates, which reduce the salience of the stimulus during preexposure, thereby allowing more effective filtering of that stimulus, and the other inhibiting the subsequent detection of the CS-UCS contingency. Accordingly, our enhanced LI in smokers compared with nonsmokers might derive from such cholinergic mechanisms. Because our subjective data provide no evidence that smokers and nonsmokers differed with respect to their interpretation of the low (and high) intensity stimuli, it seems unlikely that the reduced salience of these stimuli was responsible for the enhanced LI in smokers, although the subjective data might be an inadequate measure of salience. Thus, the enhanced LI in smokers might stem from their reduced ability to detect the contingency between the stimulus and the consequence, a phenomenon that appears to be most prominent when LI in the nonsmoker control group is more robust. The mechanisms that mediate the interactive effects of procedural parameters and being a smoker or not, which are presumed to be of long-term effect, on LI remain to be elucidated.

With respect to general effects of procedural parameters on LI, the present studies indicate that auditory LI was independent of the number of preexposures and negatively related to the intensity of the preexposed stimuli. Although statistically the latter was valid for smokers only, the descriptive statistics suggest a similar trend for nonsmokers, becausse the difference between PE- and NPE-mean AUC (corresponding to the area enclosed by the two survival curves) was larger for low (28 = 50 – 22) than high intensity stimuli (15 = 23 – 8). The lack of significant LI for nonsmokers in the "30 high" study also points in this direction. These findings appear to contradict traditional views about LI, namely that LI is a positive function of the intensity of the preexposed stimuli [reported from animal studies only: (5,27)], and a positive function of number or duration of preexposures [humans: (1,8); animals: (6,7)]. Both relationships are supposed to reflect a strengthening of the association between the preexposed stimulus and inattention, thus enhancing LI (19). For adult humans, the relationships might be changed due to humans' tendency to attribute meaning to any stimulus presented in an experimental setting (24). In fact, many high intensity noises were widely interpreted as being recorded/presented intentionally (to distract subject's attention from the masking task), whereas few low-intensity noises were interpreted as interference on the tape (caused by bad recording or age of the tape). Thus, more intense stimuli might attract more attention, if attention is not diverted by a demanding masking task, and be processed in a controlled rather than automatic manner. Such automatic processing of the preexposed stimuli seems to be necessary for the development of LI in adult humans (20). With respect to number of stimuli, two processes might be at work that counteract each other: on the one hand, attention may decrease with repeated stimulus presentation (19). On the other hand, the demand characteristics of experimental stimuli may increase with repeated stimulus presentation.

Summarizing the results, the present studies revealed enhanced LI in smokers compared with nonsmokers when using preexposure stimuli of low intensity, but similar LI when using stimuli of high intensity. In line with similar differences for acute nicotinic effects on LI in animals, the effect of smoking on LI appears to increase with the robustness of LI in the control group.

Generally, LI was found to be greater for low- than high-intensity stimuli and to be independent of number of preexposures. Although these findings contradict those obtained in animal studies and in part also in human studies, they appear to underline the importance of automatic processing of the preexposed stimuli for the development and amount of LI. Variations of preexposure parameters that might increase LI in animals might instead lead to controlled processing in human adults, thus reducing LI.

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