

What's new in *Nicotine & Tobacco Research*?

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Commentary

The mental 'lift' – absolute or withdrawal relief?

The inaugural issue of this journal (Vol. 1, No. 1, p. 45) reported on research that raised provocative questions about improved mental functioning among smokers who abstained for 18 h and then were allowed to smoke again. In their commentary in this issue, Pritchard and Robinson (p. 217) enter the debate with their own questions about both the study's methodology and its authors' interpretation of results. They point out that cognitive improvement associated with nicotine use after an 'overnight' abstinence need not be the result of relief from nicotine withdrawal, as the authors concluded, but rather an absolute effect of nicotine, as other research supports, or a combination of the two. They outline two strategies to determine which is at play for any given test of nicotine's effect on mental skills: (1) directly compare nicotine's effects on non-smokers, abstaining smokers and non-abstaining smokers. If performance is improved equally among all three groups, then nicotine is having an absolute effect; if effects are seen only among abstainers, then withdrawal relief is at work; and if all three groups are affected, but abstainers more so than the others, the effect is caused by a combination of the two. (2) Because withdrawal symptoms are transient and will resolve over time, track the performance effects of nicotine abstinence over a period of time and compare it both to performance before and after the abstinence period and to a control group not required to abstain. Just how much abstinence time is needed to get valid answers remains unknown, the authors note, but "overnight abstinence" designs cannot distinguish possible withdrawal deficits from the removal of absolute facilitation.'

Original articles

Mapping the road of good intentions

Researchers have long recognized the value of predicting which smokers are most likely to quit over the succeed-

ing year or two. For one thing, it enables development of strategies to bring smokers to that predictive doorstep. Now Herzog *et al.* have replicated and expanded on research, published in 1996, that called into question earlier findings that the best predictor is how far along a given smoker is on the continuum of 'stages of change' – a progression from having no plan to quit, to planning to quit within 6 months, seriously planning to quit within 30 days, and whether or not the smoker quit for at least 24 h during the past year.

The current findings (p. 223), based on 2-year follow-up surveys that measured 19 variables among 2379 smokers, indicate that although the 'stage of change' does have some predictive value, variables measuring nicotine dependence (for example cigarettes per day) and self-efficacy were more potent predictors of quitting. The authors conclude that 'Readiness to change should continue to be an important theme in tobacco dependence research,' but caution that 'researchers and clinicians should not uncritically assume that the stages are the optimal way by which readiness can be measured.'

Patch may help women despite PMS

Differences in nicotine sensitivity and withdrawal symptoms between men and women may result in part from the influence of ovarian hormones, the levels of which vary with menstrual cycle phases, but attempts to chart the effects of menstrual phases on nicotine withdrawal symptoms have produced contradictory results. Allen *et al.* (p. 231) now report on their testing of 30 women smokers over two 1-week periods. The women abstained from smoking for 5 days during both the high-estrogen pre-ovulation phase and post-ovulation late luteal phase, when progesterone levels are high. At random, 16 of the women received nicotine patches and 14 received a placebo.

Results from a battery of tests showed that the nicotine patch produced significant reductions in nicotine craving, premenstrual pain and affect, and premenstrual water retention and weight gain. All of the benefits were greatest when the women were in their late luteal phase.

Further research is needed to determine whether nicotine patches can similarly help alleviate premenstrual symptoms in either non-smokers or women smokers who do not abstain, and whether those benefits might prompt more women to attempt to quit smoking. At minimum, the researchers note, 'Our results. . . suggest that use of a nicotine patch may reduce or eliminate the need to factor cycle phase into decisions about the timing of smoking quit dates in women.'

Proving abstinence by enzyme activity

In research conducted with smokers, it is customary to verify whether they have abstained by measuring the cotinine in their blood, a reliable marker of nicotine intake. However, the half-life of cotinine is barely 15–20 h, so it cannot reliably indicate whether a smoker has smoked much earlier than that. Moreover, it does not reflect a biological effect of smoking. Berlin *et al.* (p. 243) suggest that, if further studies confirm, measuring the activity of the enzyme monoamine oxidase B (MAO-B), in blood platelets may give such reliable evidence over much longer periods. Cigarette smoke irreversibly cuts MAO-B activity in half. When a smoker quits, that activity returns to normal only as damaged platelets are eliminated and replaced by those not affected by smoke. This takes days: platelets have a lifespan of about 10 days, with a half-life of about 4 days, thus evidence of smoking would remain in the blood several days. Berlin *et al.* demonstrated by measuring both the plasma cotinine concentrations and MAO-B activity in platelets taken from 85 regular smokers that they are closely correlated: the higher the cotinine, the lower the MAO-B activity. MAO-B activity may play a large role in cigarette smoking's reinforcing effects, because it metabolizes dopamine and other neurotransmitters. When cigarette smoke inhibits that metabolism, higher mood-enhancing dopamine concentrations result.

Patches help cut weight gains for Hispanic women

Although some studies have shown that nicotine suppresses appetite, others find only a modest effect, if any. One shortcoming of such clinical trials of smoking cessation, however, has been that most studies include primarily non-Hispanic Whites. Now Hill *et al.* (p. 247) studied 108 Hispanic smokers in a 10-week smoking-cessation program to determine whether use of nicotine patches can help reduce weight gain. Half of the mostly Mexican-American smokers received nicotine patches, while the others received placebo patches.

The amount of weight gained for successful quitters was less for nicotine-treated females and males at 6 and 10 weeks, however, this difference was significant for females at 6 weeks only. Results of the random effects regression models (adjusted for baseline smoking characteristics) indicated that the nicotine group gained weight at a significantly lower rate than the placebo

group for females, but not for males. Gender differences regarding the effectiveness of nicotine replacement in suppressing weight gains were found in this sample population; however, further studies need to confirm these findings in other sub-groups of Hispanic smokers.

Smoking may not cause irreversible susceptibility to nicotine

One way to test whether smoking irreversibly changes smoker's brains is to test whether nicotine has stronger attraction among smokers who have quit than among people who have never smoked regularly. In 1989, Hughes *et al.* themselves published pilot studies that supported this idea. Now, however, they dispel it (p. 255) with results of a more rigorously controlled, double-blind comparison of 30 individuals – nine former smokers, 11 'never-smokers' and 10 current smokers – instructed to chew low- and high-dose nicotine gums or a placebo three times a day for 3 days.

The researchers found no significant differences between never-smokers and former smokers on 21 measures, including their preferences among the gums, how much they valued nicotine gum, and how much nicotine gum they chewed when free to increase consumption if they wanted to.

The findings suggest that using nicotine to treat patients with Alzheimer's, Parkinson's, ulcerative colitis and other conditions may not require different dosages for former smokers than for never-smokers. More significantly, the findings contradict the idea that former smokers retain an increased susceptibility to nicotine from either genetic predisposition or nicotine's presumed irreversible brain changes.

Who's hooked? Matching dependence to consumption

More people are addicted to nicotine than to alcohol, marijuana or cocaine, but little research has examined how much smoking it takes to 'hook' a smoker. Kandel and Chen (p. 263) have analyzed data from the 1991–93 National Household Surveys on Drug Abuse as an important step in answering that and, more important, how this association varies by gender, age and race or ethnicity. They matched 22,292 smokers' demographic data with their responses both on how much they smoked during the month before the survey and on six diagnostic criteria for substance dependence during the previous year. Some key findings:

1. How many cigarettes are smoked daily is the single most important predictor of likely dependence. The risk of dependence rises sharply as the number of daily cigarettes increases to half a pack a day; after that the increased risk is minimal.
2. Although more men smoke – and are heavier smokers – than women, more women smokers are 'hooked.'

The gender gap, not noticeable in adolescence, increases with age.

3. Adolescents smoke fewer cigarettes but have the highest rate of dependence at any given level of consumption. For them, how long they have been smoking is the most important predictor of dependence, but its significance declines with age.
4. Whites are more likely to be both heavy smokers and nicotine-dependent than Blacks or Hispanics. Almost three times as many Whites as Blacks or Hispanics smoke two or more packs a day.

Given such differences, the authors urge that variable, group-specific criteria be developed to identify who is at risk for nicotine dependence.

Matching smoker types to withdrawal symptoms

Not every smoker responds to withdrawal with the same symptoms, but neither are those symptoms distributed randomly across the smoking population. Pomerleau *et al.* (p. 275) surveyed 365 male and female smokers who had been recruited for laboratory studies seeking to match the withdrawal symptoms they had experienced with their scores on diagnostic tests for depression, anxiety, eating disorders, and nicotine dependence, all conditions known to be associated with smoking.

They found that, while those who suffer from depression are at increased risk of being depressed when they cannot smoke, and those with eating disorders have a higher risk of increased appetite and weight gain, anxiety and nicotine dependence *both* increased the likelihood of an array of withdrawal symptoms that include irritability, anxiety, difficulty concentrating and restlessness. To these, nicotine dependence also added craving and insomnia, symptoms that do not necessarily include cognitive/affective components.

These findings support the notion that persons with depression, anxiety, and eating disorders use smoking to self-medicate themselves, but that other processes are at play among smokers with high nicotine dependence. Another important implication, the authors note, 'is that patterns of withdrawal symptomatology may serve as useful guides for the next generation of genetic studies.' A clearer understanding of which smokers suffer which withdrawal effects might significantly improve cessation treatment outcomes by helping to match treatments to the

characteristics – and withdrawal symptoms – of smokers seeking help in quitting.

Brief report

Recruiting: what works best?

Recruiting eligible test subjects for intervention trials without depleting research budgets is a persistent problem, but little has been published to help researchers find the best recruiting methods. McIntosh *et al.* (p. 281) have now analyzed the results of seven strategies they used in recruiting 1972 smokers aged 50 and older for a smoking cessation trial. They found that:

1. Although fewer than half of those who responded to newspaper advertisements met the study's criteria and were ultimately enrolled, newspaper advertising was by far the most reliable and cost-efficient of the seven methods, accounting for 1310 (56%) of the total 2329 responses that resulted in enrolled test subjects. (Some volunteers responded to multiple solicitations.)
2. Referrals (primarily by physicians), brochures (passive recruitment), and media coverage accounted for another 15.5, 13.4 and 11.3% of the enrollee responses respectively; combined with newspaper ads, they accounted for all but 3.6%.
3. Recruiting at health fairs and other public events proved the most costly – \$143 per enrollee, compared to \$18–19 per enrollee spent on newspaper advertising or brochures.
4. Along with face-to-face recruiting at fairs, targeted mailings and HMO newsletters also proved minimally effective.

Lessons learned in one geographic and cultural setting may not succeed elsewhere, of course, and what works well in recruiting smokers who are older than 50 may not work nearly as well for other populations, but to the extent that the findings can be generalized, the authors conclude that 'paid newspaper advertisements, accompanied by 'passive approaches' (particularly physician office brochures), free media, and naturally occurring referrals, can form the basis of a campaign to successfully recruit a large number of subjects in a diverse geographic area.'