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Cigarettes & Alcohol: BFF in the Brain

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Until indoor smoking bans started popping up in cities across the country in recent years, smoke-filled bars were a fixture of American culture, smoking and drinking entwined like the peanut butter and jelly of vices. If you were a casual scientist of the street, you might have hypothesized that there was something meaningful behind the common sight of the barfly with a drink in one hand and a cigarette in the other. And laboratory research has mostly supported that anecdotal evidence, with study after study showing that alcohol does in fact promote smoking behavior, while larger surveys have found alcoholics more likely to be smokers and vice versa. But where do the effects of a beer and a cigarette meet in the brain, such that ordering up one raises a person's desire to partake of the other?

That's been one of the questions studied in the Clinical Addictions Research Laboratory at the University of Chicago Medical Center, where director Andrea King, Ph.D., an Associate Professor in the Department of Psychiatry and Behavioral Neuroscience, has examined the phenomenon of alcohol-induced smoking. The studies put the spotlight on an interesting population of smokers - not the pack-a-day regulars, but those who smoke "socially," a few cigarettes on nights out on the town with friends. That's a demographic

that hasn't received as much study as addicted smokers, King said, in part due to psychiatric guidelines that classified people as either smokers or non-smokers with no space for people in the gray areas.



"Older studies wouldn't even ask how frequently subjects smoked; if they smoke, they must be addicted, daily smokers," said King (left). "But we see this percent that seems to be increasing in subsequent surveys...about 20-30 percent would be non-daily smokers. Some of these people may continue and become vulnerable to being a chronic habitual user, or this may be a new subclass of smokers." King was drawn to social, alcohol-induced smoking behavior when she was attempting to recruit heavy drinkers who were not smokers for a control

group a task she found exceptionally difficult. With rates of smoking among alcoholics as high as 75%, the non-smoking drinker was a rare breed, so King decided to flip it around to study what causes the two behaviors to frequently co-exist.

Behavioral studies in King's lab confirmed that smoking increased people's self-reported urge to smoke as well as the number of cigarettes actually smoked. But last week, the first jump from behavior to brain activation was published by King, with University of Chicago colleagues Patrick McNamara, Michael Angstadt and K. Luan Phan in the journal *Neuropsychopharmacology*. In the study, heavy drinkers (defined as consuming more than 10 drinks a week, including at least one "binge" session of at least 4 or 5 drinks) but light smokers (fewer than 50 cigarettes each week, with non-daily frequency) were given a Kool-Aid and ethanol mixture or a placebo drink, then placed in the fMRI machine and shown two types of pictures classified like an old restaurant's seating plan: smoking and non-smoking.

The setup allowed researchers to test out two ideas about why drinking increases smoking behavior - the alcohol could make smoking cues more meaningful (the "Wow, that cigarette looks great" theory) or make people less inhibited (the "I wouldn't normally smoke, but what the heck" theory). Or both, as the two theories are not mutually exclusive. Fortunately, both of those effects have been associated with particular brain areas - activation of an area called the ventral striatum is seen when people are craving drugs or other rewards such as food or sex, while decreased activity in an area at the front of the brain called the orbitofrontal cortex is associated with impulsive, less inhibited behavior.

Despite the intimidating setting of the fMRI chamber - a claustrophobic experience of being encased in a giant metal tube - subjects still reported an elevated urge to smoke for as long as 90 minutes after drinking alcohol vs. a placebo drink. That alone spoke volumes about how powerfully alcohol pushed people to smoke, King said.

"It's so artificial [in the fMRI], but there's still an increased desire to smoke as function of drinking or placebo," King said. "It's so robust, you don't even have to be in a party or a bar."

As the subjects sat in their tube craving a cigarette, their brains showed a ripple of activation that helped the researchers sort between theories of alcohol-induced smoking. Alcohol, by itself, increased activation in the ventral striatum, and when pictures of people holding, lighting or smoking cigarettes were shown, the striatum became even more excited. That offers support for the first theory - alcohol may make the sights and smells of smoking more appealing than they would be in otherwise sober conditions, leading casual smokers to bum a cigarette and light up.

Smoking bans may have pushed some of these cues away from social smokers as they sit inside the bar, but King said that their awareness of the crowd of smokers pushed outside to the sidewalk could be a subtle cue nonetheless.

“The ban is helping workers in the bar from being exposed to secondhand smoke, but it’s not necessarily changing behaviors,” King said. “After 4 or 5 drinks, activation in striatum will still make you want to go out outside and take your smoke. The cue two years ago might be a person right in front of you, but now you know they’re out there.”

Another recent paper from King’s lab suggested that men and women may be differentially sensitive to alcohol’s magnification of these social triggers - women given an alcohol drink reported an increased urge to smoke, but did not actually smoke more when given cigarettes in a laboratory setting. And the same study found that it may not be the nicotine that drinkers are craving, but something more abstract about the act of smoking - subjects who smoked while under the influence chose a regular cigarette and a denicotinized cigarette in equal measure. But characterizing what happens in the brains of people who smoke only on social occasions, rather than all-day, every-day, could help clinicians reach and treat a previously-unrecognized population of smokers that could still be risking serious health consequences.

“While someone who is a light smoker, or non-daily smoker, might believe they are reducing their risk for lung cancer, heart disease, and all the other aspects of smoking that prematurely kill people, this may not be the case. They may compensate on a subconscious level by inhaling more deeply or closing off the ventilation holes in a cigarette and exposure themselves to similar amounts of nicotine and cancer-causing chemicals as in regular daily smokers,” King said. “There’s no such thing as a safe level of smoking.”

See: King A, McNamara P, Angstadt M, Phan KL. Neural substrates of alcohol-induced smoking urge in heavy drinking nondaily smokers. *Neuropsychopharmacology* 35:692-701, 2010. [To see a copy of this article, place this link in your browser:](http://www.nature.com/npp/journal/v35/n3/pdf/npp2009177a.pdf)

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