Proposal for New Criteria for the Diagnosis of Nicotine Addiction

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I have been conducting research on smoking for 30 years. The following recommendation is based on 40 studies our group has conducted to discover the pathophysiology of nicotine addiction. While most of these studies have been published, about a dozen of our most recent studies are still in press or under review, so much of this material, including some of the terms, will be unfamiliar to you. The DSM-III, III-R and IV nicotine dependence criteria were published without the APA having done any research to establish their validity. The criteria that I will recommend are based on the results of 13 years of continuous research involving over 20,000 individual interviews, 3 long-term prospective studies and dozens of surveys of a total of about 50,000 individuals. Through this effort we have been able to establish the pathophysiology of nicotine addiction beyond any reasonable scientific doubt by replicating all of our findings at least once. At last it is possible to derive a definition of nicotine dependence from an understanding of the disease process. However, to understand the pathophysiology of nicotine addiction it is necessary to first put aside the assumption that DSM-IV describes the core features of the disease, for it does not.

Based on the pathophysiology of nicotine addiction, which will be explained below, it is possible to define nicotine dependence in 20 words, with a single criterion.

Nicotine dependence can be diagnosed when a patient experiences a recurrent and periodic wanting, craving, or needing for tobacco.

As no other condition shares these symptoms, this presentation is pathognomonic for nicotine dependence. The following pages explain the pathophysiology of nicotine addiction. A bibliography is appended.

Addictive drugs as a class share only a single property that distinguishes them from all other drugs: they implant an unquenchable desire to repeat their use. Of course people desire many things, so it is necessary to distinguish addiction from ordinary, everyday desires. This is easily done. The desire that is the primary manifestation of addiction is **recurrent** and has **periodicity**. Recurrent means that the desire returns over and over again and never stops unless the use of the drug is curtailed. This alone distinguishes the desire that stems from addiction from ordinary desires which come and go as we grow bored with one thing and develop new interests. People do not forget to smoke because they have lost interest in it.

The second defining characteristic of addiction is that the recurrent desire has **periodicity**. Satisfying the addiction by taking the drug is like hitting the snooze button on an alarm clock. It does not end the desire, it only resets the timer, relieving the desire for a limited period of time. This essential feature has escaped the notice of researchers because of a long-standing tendency to conflate addiction with daily use. (The Diagnostic Interview Schedule instructs users not to assess dependence in nondaily smokers). Imagine a snooze button that allowed you to sleep an extra 30 days before you had to get up to go to work. When addiction begins, a single dose of nicotine can hit the snooze button on desire for weeks. Researchers have long labored under the misconception that nicotine was like the vast majority of drugs, in that it its effects disappeared when it had been removed from the body. Nothing could be further from the truth. Basic science research establishes that a single dose of nicotine can change the brain in ways that persist for days, weeks or months. It is perfectly logical then that in novice smokers the periodicity of the desire for nicotine might be measured in weeks, rather than minutes.

Desire varies over a spectrum of intensity. The desire to smoke can vary between individuals, and at different times in the same individual. English-speaking smokers commonly use the words "**wanting**" "**craving**" and "**needing**" to describe this spectrum. **Wanting** does not differ in intensity from the wants we experience throughout the day for food or beverages. It is often mild, short-lived and fairly easy to ignore. However, **addictive wanting** can be distinguished from ordinary wanting by either of two characteristics. The first is its **periodicity**, and the second is its **perceived source**. Smokers frequently perceive the source of their addictive wanting as someone or something inside their head giving them instructions. There is a big difference between saying, "I feel like eating pasta for dinner" and "I feel like someone inside my head is telling me I need to eat pasta." Smokers are right, something in their brain is telling them to smoke.

Smokers frequently use the terms "**craving**" or urges to describe a desire that is more intense than wanting. Craving can be distinguished from wanting by virtue of its being **intrusive** and **persistent**. While wanting often waits until the smoker is bored or unoccupied to make itself known, craving interrupts the smoker's concentration. Wanting will go away if ignored, but craving is like an annoying biting fly, it presents a persistent distraction.

Smokers often use the word "**needing**" to describe their predicament when they are so disrupted with craving and other symptoms of nicotine withdrawal that they cannot function normally. They don't need to smoke to get high, or to feel better than normal, they need to smoke just to feel normal again and they know they will not feel normal until they smoke. Smokers never use the term nicotine withdrawal; they say they need a cigarette.

We have collected the first case-series of patients with nicotine dependence. Smokers' case histories reveal that wanting, craving and needing typically develop in that order. According to

one adolescent, "at first you smoke because you want to, but then you smoke because you need to." So typically, addictive wanting is the earliest symptom of addiction, craving is next and needing is third. When addicted smokers are unable to smoke, the first symptom they will experience is wanting, if they do not smoke the wanting progresses to craving which in turn evolves into needing. **Wanting-craving-needing** can be understood to be the clinical manifestations of a pathological process that varies in intensity over the spectrum from wanting to needing. For the reasons that will be detailed below it will be seen to be the single core feature of nicotine addiction.

Animal studies show that one dose of nicotine changes the brain, probably forever. In novice smokers, addictive wanting for nicotine can appear after they have smoked a single, unpleasant cigarette. The largest study of nicotine addiction ever conducted reveals that about one quarter of all youth experience wanting after smoking two cigarettes and the risk of developing this symptom increases predictably with each additional cigarette smoked.

The term **latency** is used to describe the delay between finishing one cigarette and experiencing wanting, craving or needing for another. There is a **latency to wanting**, a **latency to craving**, and a **latency to needing**. Thus, addicted smokers can tell you how long they can go without smoking before they will experience wanting, how much longer it will take for craving to appear, and how long after that it will be before they need a cigarette.

Three crucial insights were required in order to establish the pathophysiology of nicotine addiction. The first is that **wanting-craving-needing has a periodicity** that may be buried within the smoker's usual pattern of smoking. The second is that when addictive wanting first appears, its **latency can be very long**. Smoking a single cigarette will hit the snooze button for weeks. The periodicity is so long, in fact, that many smokers are unaware at first that their

wanting has a periodicity, and therefore, they do not distinguish their addictive wanting for cigarettes from the ordinary wanting they experience for foods and non-alcoholic beverages. Ordinary wants do not have any such periodicity. This periodicity allows us to identify addiction when the symptoms are so mild that we would not recognize it as such. The third insight is that **the length (duration) of the latency typically shrinks over time**. At age 12, the cravings may come only once every week, by age 13, they may come once a day, and by age 14, they may be coming every few hours. Many smokers are not aware that their wanting, craving and needing has a periodicity until they realize that they can't skip a day. The shrinking of the latency is the only form of nicotine tolerance that has been tied to addiction.

Wanting-craving-needing explains why smokers find it difficult to quit, it signifies a loss of autonomy over smoking. They are free to smoke whenever they want to, but they are not free to quit whenever they want to because wanting-craving-needing makes it a difficult and unpleasant undertaking. Wanting-craving-needing puts an outside limit on how far apart cigarettes may be comfortably spaced. One may think of cigarettes that are smoked out of necessity because wanting-craving-needing demands it as '**compulsory**' cigarettes, and those smoked at other times as '**electives.**' Elective cigarettes may be smoked for relaxation, for pleasure, to fit in, to socialize, to bond with peers, to cope with stress, or out of habit. As each of the first 100 cigarettes appears to strengthen the addiction, electively smoked cigarettes contribute to the development of addiction by triggering the latencies to shorten. On average, smokers indicate that half of the cigarettes they smoke are compulsory and half are electives. A smoker who is trying to cut down to quit will first eliminate the electives and may hit a plateau when only the compulsory cigarettes remain.

Compulsory smoking rules the smoker's life. Novice smokers with long latencies can get by bumming cigarettes from their friends who carry packs, but as their latency shrinks down to a duration of one day, they must plan for how to get through days when their friends are not around. As the latencies shrink more, the smoker learns **strategic smoking**, meaning that cigarettes are smoked to reset the snooze button just before they enter a situation in which they will not be able to smoke. For kids, this is before school; for adults, before work, before going into a restaurant, an airport or theater. Before an anticipated period of forced abstinence, a smoker may smoke two cigarettes in rapid succession, or smoke more of the cigarette, or take longer, deeper drags to obtain more nicotine from their last cigarette in attempt to prolong the latency.

Recent clinical work indicates that our current definitions of **nicotine withdrawal** are lacking in certain aspects. Withdrawal has been previously defined on the basis of a presumption that withdrawal symptoms must appear soon after discontinuation of use, increase in intensity and then fade away. This restricted definition does not accurately reflect the clinical presentation of nicotine addiction because it only describes a limited range of the clinical presentation.

A different picture emerges if we define withdrawal as any symptom that results from the discontinuation of nicotine's pharmacologic action without making presumptions about timing and changes in intensity. By this definition, **periodic addictive wanting** is the earliest and most commonly experienced nicotine withdrawal symptom. The fact that addictive wanting has a latency identifies it as a withdrawal symptom: it reliably appears at a predictable interval following the last dose of nicotine. During a period of abstinence, **wanting** is followed by **craving**, and then by **needing** a cigarette to feel normal again. Smokers may feel they need a cigarette to feel normal because they are experiencing such withdrawal symptoms as irritability,

impatience, restlessness, difficulty concentrating, nervousness or disturbed sleep. If we incorporate these DSM symptoms of nicotine withdrawal into our definition of needing to smoke to feel normal, **wanting-craving-needing can be seen to encompass the spectrum of symptomatic nicotine withdrawal**.

When addiction begins, addictive periodic wanting may be the only symptom of nicotine withdrawal that a smoker experiences. It is possible that smokers undergo subclinical withdrawal between cigarettes, disturbances in normal neurophysiologic functioning that do not produce recognized symptoms. Once we are able to identify the neurophysiologic processes that underlie nicotine withdrawal, noninvasive techniques such as functional MRI may make it possible to identify the asymptomatic phase of withdrawal that precedes wanting.

If given the opportunity, withdrawal will emerge after every cigarette for the rest of the smoker's life. Inveterate smokers may learn to recognize the onset of withdrawal subconsciously, lighting up a cigarette even before they are aware that they want to smoke.

As the latencies shorten, smokers develop a number of behaviors that have long been recognized as signs of addiction, but without an understanding of their pathophysiology, and hence, no explanation for why that would be the case. For example, latencies impose regularity which is recognized by some as a sign of addiction. If their **latency to needing** is less than 8 hours, they may find they need to smoke with 5 minutes of arising, or that the first cigarette of the day is the one they would most hate to give up. All of these are late secondary signs of addiction, and they are explainable as signs of addiction when it is understood that they are manifestations of the **wanting-craving-needing symptom complex** with its latencies.

The wanting-craving-needing symptom complex underlies most of the behaviors that are included in the DSM-IV nicotine dependence criteria. (1) *Tolerance, defined as a need for*

markedly increased smoking to achieve the same effect, or markedly diminished effect with continued use, is a symptom of addiction only if it is measured in terms of a shortening of the latencies. A cigarette that would have provided weeks of relief from symptoms of wanting-craving-needing in the novice smoker may provide only a few minutes of relief in the inveterate smoker. (2) *Smoking in larger amounts or over a longer period than intended.* As the latencies shorten, smokers find that they must smoke more often to relieve their symptoms. (3) *Unsuccessful efforts to cut down or quit.* Wanting-craving-needing makes it difficult to quit. (4) *Withdrawal symptoms*. These are a manifestation of the needing aspect of wanting-craving-needing. (5) *A great deal of time spent obtaining or using tobacco*. As the latencies shorten, smokers must spend more and more time smoking just to feel normal. (6) *Important activities given up or reduced because of smoking.* Smokers begin to avoid places or situations that will prevent them from smoking when their latencies demand it. Smoking becomes a priority over other activities because they need to smoke just to feel normal. (7) *Use despite physical or psychological problems caused or exacerbated by smoking.* Smokers cannot forgo smoking even when they are sick because the onset and progression of wanting-craving-needing makes them feel even worse. Although this paragraph may sound like a justification for retaining the DSM-IV, that would be a mistake, as five of these (all except tolerance as I have defined it, and withdrawal) are late secondary manifestations of addiction that have no particular significance to the pathophysiology. DSM misses the boat when it comes to assessing the single core feature of wanting-craving-needing.

Not only does the wanting-craving-needing symptom complex explain such secondary symptoms of dependence as regularity, prioritization, and giving up other activities, it predicts the progression of the illness of nicotine addiction with **extreme sensitivity and specificity**.

This is something that the DSM cannot do. Although symptoms of wanting-craving-needing may appear in youth who smoke only a few cigarettes per month, the presence of such symptoms increases the likelihood of persisting with smoking and progressing to heavy smoking by a factor of nearly 200 fold. This indicates a sensitivity of about 99% in the ability to predict an ominous trajectory of tobacco use based on symptoms that may appear after smoking one cigarette. Conversely, there is no addiction in the absence of wanting-craving-needing. We can state with 99% certainty that youths who do not develop wanting-craving-needing will not progress to heavy smoking (99% specificity). This is because essentially nobody progresses to heavy daily smoking unless it is a result of wanting-craving-needing. The predictive power of this symptom complex exceeds that of the vast majority of laboratory tests used in clinical medicine. No other smoking risk factor approaches this level of predictive power. In fact, wanting-craving-needing leaves almost no variance for other factors to explain. It is on this basis that **wanting-craving-needing can be identified as the core or defining feature of nicotine addiction**. The wanting-craving-needing symptom complex can be identified as the single essential feature of addiction because it is sufficient alone to predict with astounding accuracy the clinical course of addiction, and to explain a broad spectrum of addictive behaviors.

Periodic wanting-craving-needing is **pathognomonic** for nicotine addiction, that is, there is no other condition that produces these symptoms. Therefore, the presence of any of these symptoms is sufficient for a clinician to make a confident diagnosis of nicotine addiction.

But shouldn't we reserve the term addiction for people who continue to smoke even though it is ruining their health? From a diagnostic standpoint, it makes no sense to identify the wanting-craving-needing symptom complex as nicotine addiction only when the non-nicotine components of the cigarette smoke have wreaked their havoc on the smoker's health. Do

smokers become addicted only when they fall ill? In medicine we want to diagnose diseases before they have caused irreparable damage, or even better, before they have produced symptoms.

We have launched an effort to disseminate our new knowledge about the pathophysiology of nicotine addiction and its diagnosis to the lay public, to physicians and other healthcare providers. We are seeking to have this knowledge incorporated into the coming editions of primary care medical textbooks. The DSM-IV committee had an impossible task because the pathophysiology of nicotine addiction was not understood at that time. The pathophysiology of nicotine addiction is now very well established even if it is not yet understood beyond a small circle of researchers. As I said, the final pieces in this puzzle are still in press. I am writing to you and the ICD committee in the hope that we can all work together to ensure that your next set of criteria will accurately reflect the current state of medical science.

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