

Warburton Review & comments by Rothman's.

In general, both the review & comment are better than we have had previously. This, however, is not a great compliment as previous essays have been too simplistic or even wrong in many respects.

I have to take exception to certain points: I have indicated where this occurs in Rothman's summary, ^{the summary is an accurate representation of the review} but ~~the review~~ ^{the review} must be doubted that smokers are sensitive to all their blood nicotine levels. I also doubt that ^{all} smokers consciously vary their inhalation pattern ^{to adjust delivery under various conditions}. Such adjustment may be unconscious i.e. puff faster when nervous, but Warburton clearly implies that smokers consciously manipulate their nicotine levels.

b) Where is the evidence for breathing pattern alteration under different circumstances? Tests in laboratories have not demonstrated such changes - albeit in abnormal smoking surroundings - and no sophisticated monitoring data on inhalation patterns is, as yet, available so far as I know.

c) The references for nicotine enhancement of learning and of concentration are very selective. Many workers (not Warburton) find the nicotine does enhance these parameters versus deprived smokers but only up to the level of non smokers, there is no added advantage of nicotine per se.

d) The suggestion that ^{relatively} low blood concentrations of nicotine can give ^{effective} brain concentrations without risk of toxicity to other organs is

101000609

mistaken. It is suggested that this is accomplished by the high blood flow to the brain & rapid uptake of nicotine from blood into the brain. The most obvious objection to this is the gross blood supply to both kidney and liver - at least as high as that to brain - and so, presumably, at risk. Also, calculations of a required blood concentration to permit an effective brain conc demand knowledge of what an "effective brain conc" of nicotine is. We don't know this.

d) Warkentin vacillates between the importance of the direct action of nicotine (i.e. actually on nicotinic ACh receptors) and the indirect action (i.e. nicotine, via nicotinic ACh receptors, releases some other hormone or neurotransmitter which then causes some effect.)

Both actions obviously occur, though it will be clear that an indirect effect cannot occur without a direct action occurring first.

The notion that nicotine is more benign than amphetamine (for example) just because nicotine acts directly whereas amphetamine releases noradrenaline is false.

Nicotine ^{acts} is no more naturally ^{this obviously} than any other substance - even an exogenous dose of one of the body's own neurotransmitters.

e) Warkentin states tolerance does not occur to nicotine because it is so similar to ACh

101000610

and ~~tolerance~~ "cannot become tolerance to the body

(its) own transmitters".

We know that tolerance does occur to nicotine. Tolerance does not mean ever increasing doses it merely implies some sort of adaptation.

Another example of tolerance to one of the body's own transmitters is morphine or heroin dependency. These substances work because they have a chemical similarity for the ~~that~~ enkephalin / endorphin affinity receptors just as nicotine has for nicotinic ACh receptors.

(f) The idea that nicotine's actions are specific is silly. Any compound which is capable of releasing ~~any~~ all of the body's neurotransmitters (and nicotine can do this) can in no way have a specific action.

(g) The ~~fact~~ fact is not surprising that nicotine alone is not a substance of abuse. Where can the general public obtain nicotine as a pure substance?

(h) Nicotine has been reported to produce

101000611