

GABA Changes Acutely in Human Brain after Nicotine Administration

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Background

Animal studies show that nicotine enhances GABA release. Animal studies also suggest coupling of GABAergic and glutamatergic activity. While less is known about humans, we see decreased occipital GABA with total light deprivation, associated with reduced glucose metabolism, and by inference glutamatergic neuron activity. Human studies show low brain GABA in depression, which is accompanied by slower occipital metabolism. Therefore, we hypothesized that nicotine will increase the concentration of brain GABA.

Methods

6 non-depressed healthy smokers (4 men, 2 women; age = 31±8 years) were abstinent 10-18 hours, as verified with a measurement of expired CO below 15 ppm. ¹H magnetic resonance spectroscopy of brain GABA was done with J-editing (1) at a magnetic field strength of 4T before and after a Nicorette® nicotine inhaler (1-2 mg systemically available). GABA was analyzed using LCMoel (2) and quantified relative to tissue water. 10 nonsmokers completed two scans without nicotine. Brain GABA was assessed relative to tissue water, taking 10 minutes to position the voxel, shim (3), and calibrate RF powers.

Results

Smokers had Fagerström scores of 3.4±1.8 (mean ± SD), consumed 13±8 cigarettes/day, with a range from 5 to 20 cigarettes per day. Brain GABA levels increased by 10±4% after nicotine consumption (mean ± SD, p=0.004, two-tailed t-test). In non-smokers GABA levels did not change significantly (change = +2.5 ± 5.3%), no relation was found between the GABA change and cigarettes per day or Fagerström score, possibly due to the small sample size.

Conclusion

Nicotine is known to induce GABA and glutamate release. The data are consistent with the theory that glutamate and GABA release can alter brain GABA levels. The results also highlight possible links of smoking with disorders that are associated with GABAergic abnormalities, such as depression.

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References

1. Rothman DL et al. Proceedings of the National Academy of Sciences of the United States of America 1993; 90:5662-6
2. Provencher SW. Magn Reson Med 1993; 30:672-679
3. Shen J et al. Magn Reson Med 1997; 38:834-839

