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Nerve Growth Factor and Smoking Cessation

**Increase of Nerve Growth Factor serum concentration after acute smoking
withdrawal**

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Nerve growth factor (NGF) is the best characterized neurotrophin essential for neuron survival, differentiation and function in the peripheral and central nervous system [1]. In addition it is hypothesized that NGF plays a modulatory role in the immune system, is involved in the regulation of specific neuroendocrine functions [1] and is elevated in psychologically stressful situations [1]. As acute nicotine withdrawal is associated with psychological stress and an elevation of NGF has been shown also after alcohol withdrawal, [2] we hypothesized NGF to be elevated during withdrawal from smoking.

Eight female and seven male smokers (mean age 35.0 (SD 10.7) years) and 10 pair-matched non-smokers were investigated. Smokers consumed more than 10 cigarettes/day for ≥ 5 years and were medication-free within the past year. Any psychiatric and medical disorder led to exclusion from the study. The grade of nicotine dependence was measured with the Fagerstroem nicotine tolerance questionnaire.

NGF serum concentrations were measured in smokers on 3 consecutive days at the same daytime (± 15 minutes) and one-time in non-smokers. On day one and day three the smokers consumed at least 8 cigarettes before the blood was drawn, on day two they were abstinent for ≥ 16 hours. The measurement on day three was performed to detect delayed NGF changes.

No significant difference of the NGF baseline levels between smokers and non-smokers (mean, (SD): 63.4 (117.8) versus 57.3 (96.6) pg/ml; Mann-Whitney-Wilcoxon: $S=137.0$, exact p -value=0.71) has been detected. As a main finding a significant overall change of the NGF levels over the three days was observed (Friedman-test: $S=7.56$, exact p -value=0.02). Post hoc analysis revealed a significant increase of NGF levels between day two and day three (mean, (SD): 76.3 (176.3) versus 104.5 (266.4) pg/ml, respectively; Wilcoxon after Bonferroni correction: $S=39.50$, exact p -value=0.03). A positive correlation between the Fagerstroem

score and NGF baseline levels (Spearman: $r=0.53$, $p=0.04$) but not, however, with NGF changes was found.

In line with this observation, a release of NGF into the bloodstream was found in adult male mice in social isolation as well as in parachutists experiencing their first jump, suggesting psychological stress is associated with increased serum NGF [1]. Moreover high levels of serum NGF in patients during acute withdrawal from alcohol or heroine [2] indicate an involvement of NGF in addictive behavior and withdrawal distress. The positive correlation between Fagerstroem score and NGF concentration strengthens the view of a connection with addictive behavior. This study represents the first observation that NGF serum concentration is altered during acute withdrawal from nicotine although this findings must be considered as preliminary and need replication in a further study.

References

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- [2] Aloe L, Tuveri MA, Guerra P, Pinna L, Tirassa P, Micera A, Alleva E: Changes in human plasma nerve growth factor level after chronic alcohol consumption and withdrawal. *Alcohol Clin Exp Res* 1996; 3: 462-466