Project Review

"Determination of blood nicotine and cotinine concentrations before, during and after exercise performance"

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Nicotine is widely reported to increase alertness, improve coordination and enhance cognitive performance, however, only one study has to our knowledge attempted to replicate these findings to exercise capacity. We previously observed an improved exercise duration by 17% with transdermal nicotine, and in the absence of any effect on peripheral markers concluded that nicotine prolongs endurance by a central mechanism. This finding, coupled with increased anecdotal evidence of nicotine 'experimentation' amongst competitive cyclists and the fact that as yet it is neither a banned substance nor is its access restricted, raises an ethical dilemma over athletes gaining an unfair advantage and/or serious concerns over the safety of its use during competitive exercise/sport. We are currently finishing a follow-up study to determine whether nicotine administration (patch, gum vs. placebo) can improve ~1h time-trial performance in trained cyclists. The present project proposes to analyze frozen human plasma samples this study. Samples at rest, prior to and following exercise will be analysed for nicotine and cotinine, its' major metabolite, using reverse-phase HPLC. Results will shed light onto concentrations of nicotine and its major metabolite when taken in the quantities that are commonly available 'over-the-counter' in endurance-trained cyclists competing in a simulated event

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Results and Conclusions

Nicotine is widely reported to increase alertness, improve coordination and enhance cognitive performance; however, only one study has attempted to replicate these findings to exercise capacity, observing an improved exercise duration by 17% with transdermal nicotine administration. This finding, coupled with increased anecdotal evidence of ‘experimentation’ amongst athletes and the fact that as yet it is neither a banned substance nor is its access restricted, raises an ethical dilemma over athletes gaining an unfair advantage and serious concerns over the safety of its use during competitive sport and exercise.

Therefore, we conducted a follow-up study to determine whether nicotine administration can improve a 1h time-trial performance in trained cyclists, a more face-valid protocol. We recruited 10 competitive male cyclists who attended the laboratory on three occasions one week apart in a randomized order. A 48-hr period of dietary and exercise control preceded each visit, which comprised a work-dependent time-trial on a cycle ergometer to simulate 40km or about 1 hr. On one occasion they received a nicotine patch (PAT, 7 $mg \cdot 24hr^{-1}$) the evening before, on another nicotine gum (GUM, 2 mg) 30 mins prior to exercise, and finally placebo gum and patch (PLA). Venous blood samples were taken at rest, prior to and following exercise and analysed for nicotine and its major metabolite, cotinine, in plasma using high-performance liquid chromatography (HPLC).

GUM (-0.6 ± 4.4%) and PAT (-1.0 ± 4.8%) resulted in no significant improvement in performance time compared to PLA (62.9 ± 4.1, 62.6 ± 4.5 and 63.3 ± 4.1 min, respectively), with mean power outputs of 264 ± 31 (GUM), 265 ± 32 (PAT) and 263 ± 33 W (PLA), respectively. None of the variables measured (core body temperature, heart rate, ratings of perceived exertion) were different between trials. Despite concerted efforts we were unable to recover sufficient nicotine from plasma samples, most likely due to its tendency to fluctuate, relatively short half-life of about 2h, or perhaps sensitivity of the HPLC (cf. mass spectrometry). Recovery of cotinine - nicotine’s major metabolite (70%) and with a longer retention time of 18-20h - was 100% and lends itself better to accurately and sensitively assessing blood concentrations following nicotine administration. For the

baseline samples, traces of cotinine were found in 2 subjects during PLA, 2 subjects during GUM, and unsurprisingly all 10 when they had been wearing PAT overnight. During PLA, negligible concentrations were found at baseline (0.3 ± 0.3 ng/ml), pre-exercise (0.5 ± 0.2 ng/ml) and post-exercise (1.0 ± 0.6 ng/ml). During GUM, negligible concentrations were found at baseline (0.3 ± 0.3 ng/ml), pre-exercise (1.3 ± 0.5 ng/ml) rising significantly post-exercise (3.2 ± 0.8 ng/ml). During PAT, concentrations were significantly elevated compared to GUM and PLA at baseline (34.2 ± 0.7 ng/ml), pre-exercise (38.3 ± 6.3 ng/ml) and post-exercise (43.5 ± 6.3 ng/ml) but did not change over time.

On the basis of our results, i) it appears as though route and/or duration of administration affect absorption, ii) mass spectrometry is likely preferable over HPLC, where available, for sample analysis, and iii) we recommend future studies to incorporate urine analysis in addition to blood, and dose-dependent effects to be investigated.