PROJECT REVIEW

”Metabonomic signature in bike athletes: a pilot study”

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Detecting the presence of an administered exogenous substance for enhancing sport performances still represents a difficult challenge in the current approach, as it relies on the capacity of measuring quantitatively the substance or its metabolites in easily accessible biological samples and to compare these concentrations with a priori defined specific threshold. The main drawbacks remain 1) that the substance must be known a priori and detectable with current methods; 2) that the long term effects of a chronic and/ or combined administration of these substances on the homeostasis, even when these substances are no more measurable in the blood, are not taken into account.

In the metabonomic approach, a particular homeostatic domain is considered as a global system, including all its particular potential links with other metabolic systems. Multi- dimensional quantitative measurements of individual spectrum are achieved using Mass Spectrometry and NMR- Spectrometry, which are secondly globally compared to normal metabonomics profiles using multi-dimensional statistical techniques in order to detect major deviations form the normal homeostatic profiles.

Long term follow up in endurance competitors with biological samples collected during either the training- or the competition- periods over several years gives the unique opportunity of applying the metabonomic approach to a real data set of professional and elite amateur competitors.

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Results and Conclusion

The longitudinal endocrine follow-up of sportsmen performed by conventional methods allows detection of some biological abnormalities that may be related to doping practices. Use of indirect methods to phenotype general metabolism is very promising to better detect endocrine disruptions. To better know its intrinsic potential, a ^{1}H nuclear magnetic resonance (NMR)-based metabonomic study has been performed on sera (n = 649) coming from blood collected on an elite road cycling cohort (n = 250) between 20 and 33 yrs old.

Thanks to multivariate statistical analyses performed on metabolic fingerprints, metabolic signatures, which are specific of different types of endocrine disruptions related to the secretion pattern of either cortisol, testosterone or IGF-1, have been successfully produced. For every endocrine phenotype, 3 classes have been defined, i.e. low, normal and high concentrations. Prediction of a specific endocrine phenotype has been obtained from 419 metabolic variables selected from NMR fingerprints.

Validation of the assignment of a given subject to a given class has been estimated by bootstrap-based techniques using shrinkage discriminant analysis, a modified linear discriminant analysis, from metabolomic data submitted to a prior orthogonal signal correction, which is very useful to discard noisy information. The best classification performances have been obtained to predict the cortisol and IGF-1 phenotypes: 600 statistical individuals were necessary to predict nearly 100 % of test samples. Yet, for testosterone, a larger size cohort is necessary to get the same performances.
Biomarkers related to different metabolic pathways concerning lipids are regularly found for any of the 3 endocrine phenotypes examined here. Complementary bioinformatic studies are still necessary to better characterize at a biochemical side the differential metabolic disruptions linked to the different hormonal disruptions considered here.

Indeed, from this first extended metabolic exploration performed on a relatively large cohort of sportsmen, metabonomics may be routinely used to reinforce the detection of endocrine abnormalities given the fact that more robust classification rules coming from a significantly extended cohort would be thus available.

This methodology could be advantageously used in near future in conjunction with the Athlete Biological Passport, which will be used to detect haematological, steroidal and endocrine abnormalities in high level sportsmen in a longitudinal follow-up perspective.