


[Print this Page for Your Records](#)
[Close Window](#)
Control/Tracking Number: A-22-1546-EASD

Activity: Abstract

Current Date/Time: 4/1/2022 9:57:08 AM

Alpha-melanocyte stimulatory hormone (α MSH): A novel and potent regulator of glucose tolerance in humans.

Author Block: N.G. Docherty¹, P. Swan¹, B. Johnson², S. Samarasinghe³, M. Cowley⁴, C.W. le Roux^{1,5}, A.D. Miras²;

¹School of Medicine & Medical Science, University College Dublin, Dublin, Ireland, ²Department of Metabolism, Digestion and Reproduction Imperial College London, London, UK, ³Department of Metabolism, Digestion and Reproduction Imperial College London, London, UK, ⁴Monash Biomedicine Discovery Institute, Victoria, Australia, ⁵Centre for Diabetes, Coleraine, UK.

Abstract:

Background and aims: Intravenous administration of exogenous α MSH lowers glucose excursions during oral glucose tolerance testing (OGTT) in pre-clinical studies. We aimed to interrogate whether this action is preserved in human physiology, both *in vivo* and *in vitro*.

Materials and methods: Two cohorts, each of fifteen healthy volunteers received infusions of physiological saline, 15, 150, and 1500 ng/kg/hr α MSH initiated 30 minutes before administration of a standard OGTT. Plasma glucose and insulin were measured during the OGTT. To assess the effect of α MSH on skeletal muscle glucose disposal, subjects underwent sequential hyperinsulinaemic-euglycaemic clamp studies with saline and 150ng/kg/hr α MSH infusion. In a separate cohort of healthy volunteers (n=6), primary human myotubes were generated from *vastus lateralis* muscle biopsies and used to directly assess glucose uptake in response to α MSH.

Results: Infusion of α MSH (1500ng/kg/hr) led to a 45% reduction in the 2-hour incremental area under the curve (iAUC) for plasma glucose ($p<0.001$). Accordingly, plasma insulin was reduced by 20% ($p=0.006$). In clamp studies, α MSH increased glucose requirements for the maintenance of euglycaemia. Primary human myotube melanocortin receptor subtypes (MC1R>MC3R≈MC4R). A sixty-minute incubation of myotube cultures with 10nM α MSH increased glucose uptake by two-fold versus vehicle, which was equipotent to the effect obtained with insulin. The glucose uptake promoting effects of insulin and α -MSH in myotubes were additive.

Conclusion: These findings substantiate a role for peripheral α MSH as a hitherto undescribed component of the endocrine control of glycaemia in human physiology. The melanocortin axis offers a novel target for the development of diabetes pharmacotherapy.

Author Disclosure Information:

N.G. Docherty: None.

Keyword (Complete): 22 Peripheral non-insulin hormones

Study information (Complete):

*Human studies: Yes

*Animal Studies: No

Grant Acknowledgement (Complete):

Please select Yes or No: Yes

Support: : Health Research Board Ireland and EFSD Albert Renold Travel Fellowship

Clinical Trial Registration Number (Complete):

: Yes

: ISRCTN26265036

Status: Complete

European Association for the Study of Diabetes (EASD)

Rheindorfer Weg 3

D-40591 Dusseldorf - Germany

Tel: +49-211-758 469 0 - Fax: +49-211-758 469 29

Web: <http://www.easd.org>

E-mail: abstracts@easd.org

Feedback