Side-effects of anti-inflammatory steroids could be prevented, research finds

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(Medical Xpress)—Problem side effects including high blood pressure, obesity, muscle wasting, osteoporosis and skin thinning in arthritis and asthma sufferers who take a certain kind of steroid could be prevented by deleting a key gene, researchers at the University of Birmingham have discovered.

The side effects can affect anyone who takes glucocorticoids, which can also include the recipients of organ donation, who take them to prevent the organ being rejected.

The Birmingham research, published online in *Proceedings of the National Academy of Science* (*PNAS*), demonstrates that the side effects associated with glucocorticoid use are prevented in mice when the gene for an enzyme called 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) is deleted. This raises the possibility of the same effect occurring in humans.

Dr Gareth Lavery, from the School of Clinical and Experimental Medicine at the University of Birmingham said: "Our findings identify a link between the side-effects experienced by people taking prescribed glucocorticoids, and the gene 11β-HSD1 – raising the exciting possibility of using selective 11β-HSD1 inhibitors as an adjunctive therapy to reduce the side-effect profile associated with long-term glucocorticoid use."

This enzyme generates glucocorticoids, within cells and organs including

fat, liver, skin and muscle. The team have shown that the side-effects associated with therapeutic glucocorticoid use are driven by an 11β-HSD1-affected increase of glucocorticoid levels in these tissues. By deleting the 11β-HSD1 gene from a group of mice, the researchers found that the negative effects the glucocorticoid treatments were abolished. These findings extend previous observations made by the team in which a patient with defective 11β-HSD1 activity was protected from the adverse effects associated with prolonged high glucocorticoid exposure.

More information: Stuart A. Morgan, Emma L. McCabe, Laura L. Gathercole, Zaki K. Hassan-Smith, Dean P. Larner, Iwona J. Bujalska, Paul M. Stewart, Jeremy W. Tomlinson, and Gareth G. Lavery. "11β-HSD1 is the major regulator of the tissue-specific effects of circulating glucocorticoid excess." *PNAS* 2014 ; published ahead of print June 2, 2014, DOI: 10.1073/pnas.1323681111

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