

Steroid meds linked to structural and volume changes in brain white and gray matter

August 30 2022



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The use of prescribed steroids, including in inhalers, is linked to changes in the structure and volume of white and gray matter in the brain, suggests the findings of the largest study of its kind, published in the open access journal *BMJ Open*.

The associations found might help to explain the neuropsychiatric

effects, such as anxiety, depression, mania, and delirium frequently seen after long term use, say the researchers.

Their immunosuppressive properties mean that glucocorticoids, a class of synthetic steroids, are among some of the most frequently prescribed drugs. They are used to treat a wide variety of medical conditions.

The estimated annual population prevalence in [high income countries](#) of systemic (infusions and tablets) medical steroid use is thought to range between 0.5% and 3%.

While very effective, both systemic and inhaled steroids are associated with many potentially serious metabolic, cardiovascular, and musculoskeletal side effects, as well as neuropsychiatric effects.

Previously published research suggests that long term medical steroid use is associated with structural abnormalities and shrinkage of certain areas of the brain. But most of these studies have involved only small numbers of people with specific conditions.

And it's still not clear if these associations might also be observed in a broader sample of medical steroid users, including those using inhaled steroids for respiratory conditions, such as asthma.

In a bid to find out, the researchers drew on data from the UK Biobank, comprising half a million 40–69 year olds from the [general population](#), to see if there were any detectable differences in brain volume and structure between users and non-users of systemic and inhaled steroids.

The researchers also wanted to know if steroid use might be associated with differences in processing speed and emotional responses.

The MRI brain scans of 222 people using systemic steroids and 557

using inhaled steroids were compared with those of 24,106 non-users.

None of the study participants had previously been diagnosed with neurological, psychiatric or hormonal (endocrinological) disorders or was taking mood altering drugs, such as antidepressants.

Participants filled in a questionnaire to assess certain aspects of mood over the previous fortnight.

Comparison of the MRI scan results showed that both systemic and inhaled steroid use was associated with less intact [white matter](#) structure than was seen on the scans of those not on these drugs. White matter has a role in neuronal connectivity and signaling in the brain.

The effects were greater in systemic users than in users of inhaled steroids. And further detailed analysis suggested that the effects might be even larger among long term users.

Systemic use was associated with a larger caudate compared with no use, while use of inhaled steroids was associated with a smaller amygdala. Both the caudate and amygdala are [gray matter](#) structures in the brain involved in cognitive and emotional processing.

Systemic steroid users also performed worse on a test designed to measure processing speed than non-users, and they reported significantly more depressive symptoms, apathy, restlessness and fatigue/lethargy than non-users. Inhaled steroid users reported only more tiredness/lethargy, and to a lesser degree than systemic steroid users.

"Although a causal relation between glucocorticoid use and changes in the brain is likely based on the present and previous studies, the cross-sectional nature of this study does not allow for formal conclusions on causality," caution the researchers.

They also point to certain limitations. Only a few indicators of mood change were assessed, and only for the preceding 2 weeks; and the reported changes might have been related to the condition for which [steroids](#) were prescribed rather than to steroid use itself.

Nor were the researchers able to differentiate between steroid tablets and infusions for systemic users, all of which may have influenced the findings.

But they write: "While it remains unclear whether the observed effect sizes have clinical consequences for the population of glucocorticoid users as a whole, these findings are remarkable given the common neuropsychiatric side effects of synthetic glucocorticoids."

And they conclude: "This study shows that both systemic and inhaled glucocorticoids are associated with an apparently widespread reduction in white matter integrity, which may in part underlie the neuropsychiatric side effects observed in patients using glucocorticoids."

Given how widely used these drugs, both doctors and patients need to know about the possible effects on the [brain](#), say the researchers, who now call for research into alternative treatment options.

More information: Association between use of systemic and inhaled glucocorticoids and changes in brain volume and white matter microstructure: a cross-sectional study using data from the UK Biobank, *BMJ Open* (2022). [DOI: 10.1136/bmjopen-2022-062446](https://doi.org/10.1136/bmjopen-2022-062446)

Provided by British Medical Journal

Citation: Steroid meds linked to structural and volume changes in brain white and gray matter

(2022, August 30) retrieved 26 January 2024 from
<https://medicalxpress.com/news/2022-08-steroid-meds-linked-volume-brain.html>

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