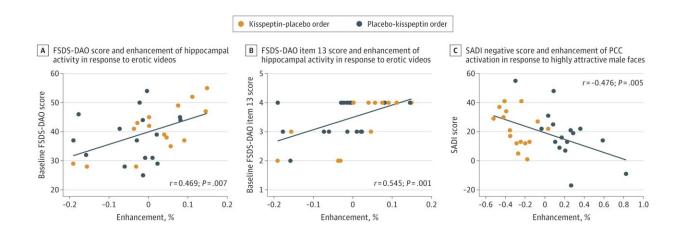


Kisspeptin hormone injection could treat low sex drive in women and men

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Correlation Analyses of Regions of Interest Activity With Measures of Sexual Aversion and Distress and Aversion. Credit: *JAMA Network Open* (2022). DOI: 10.1001/jamanetworkopen.2022.36131

The hormone kisspeptin could be used to treat women and men distressed by their low sexual desire, according to two new studies.

The studies, led by clinicians and scientists at Imperial College London and Imperial College Healthcare NHS Trust and both published in *JAMA Network Open*, found that giving kisspeptin can boost sexual responses in women and men who have <u>hypoactive sexual desire disorder</u> (HSDD)—a condition characterized by <u>low sexual desire</u> that is distressing to the individual. HSDD affects up 10% of women and 8% of men worldwide



and can have devastating psychological and social impacts.

Kisspeptin is a naturally-occurring hormone that stimulates the release of other reproductive hormones inside the body. The team have previously shown in men with intact sexual desire that kisspeptin can enhance responses to sexual stimuli, and boost attraction brain pathways, independent of other reproductive hormones like testosterone. Now, they investigated the effects in women and men with low sexual desire for the first time.

These two <u>clinical trials</u> involved 32 pre-menopausal women and 32 men with HSDD. In both studies, patients underwent scanning of the brain using MRI, as well as blood and behavioral tests. Kisspeptin administration improved sexual brain processing in both women and men, resulting in positive effects on sexual behavior compared to placebo. These are the first clinical studies to explore the ability of kisspeptin to boost sexual pathways in women and men distressed by their low sexual desire.

The researchers believe that the results lay the foundations for kisspeptinbased treatments for women and men with HSDD.

Dr. Alexander Comninos, from the Department of Metabolism, Digestion and Reproduction at Imperial College London, Consultant Endocrinologist at Imperial College Healthcare NHS Trust and co-senior author of the study, said, "Low sexual desire can be distressing and so result in HSDD. This can have a major detrimental impact on relationships, mental health, and fertility. Even though it is relatively common, treatment options in women are limited, carry significant side-effects and in some cases can be harmful to even try. And unfortunately, these treatments have limited effectiveness. In men there are currently no licensed treatments and none on the horizon. Therefore, there is a real unmet need to find new, safer and more effective therapies for this



distressing condition for both women and men seeking treatment.

"Our two studies provide proof-of-concept for the development of kisspeptin treatments, as we provide the first evidence that kisspeptin is a potentially safe and effective therapy for both women and men with distressing low sexual desire. Additionally in men, we demonstrate that kisspeptin can have positive effects not only in the brain but also in the penis by increasing rigidity. Furthermore, kisspeptin was well-tolerated by both women and men with no side-effects reported, which is crucial from a drug development point of view. We now plan to take things forward to hopefully realize the potential of kisspeptin therapeutics in psychosexual disorders—sexual problems which are psychological in origin, such as unexplained low libido."

Professor Waljit Dhillo, an NIHR Senior Investigator, also from the Department of Metabolism, Digestion and Reproduction at Imperial College London, Consultant Endocrinologist at Imperial College Healthcare NHS Trust and co-senior author of the study, added, "Our studies build on our previous work to assess the effectiveness of kisspeptin and its boosting effects in terms of arousal and attraction. It is highly encouraging to see the same boosting effect in both women and men, although the precise brain pathways were slightly different as might be expected.

"Collectively, the results suggest that kisspeptin may offer a safe and much-needed treatment for HSDD that affects millions of people around the world and we look forward to taking this forward in future larger studies and in other patient groups."

The study in women involved a randomized, double-blind, two-way crossover, placebo-controlled trial at Invicro and Hammersmith Hospital (part of Imperial College Healthcare NHS Trust), between October 2020 and April 2021. Data analysis was carried out by Imperial College



London researchers.

Thirty-two pre-menopausal heterosexual women with HSDD (aged 19–48 years) completed two study visits, one for administration of kisspeptin and another visit for placebo. Participants completed psychometric questionnaires before and towards the end of kisspeptin or placebo administration to assess their mood and behavior. During kisspeptin or placebo administration, participants underwent functional MRI while watching erotic videos and viewing male faces to see how brain activity was affected. Non-erotic exercise videos were used as a control.

The team found that kisspeptin improved sexual and attraction brain activity in key brain areas in women. They also found that women who were more distressed by their sexual function showed greater kisspeptinenhanced brain activity in the hippocampus (a key structure implicated in female sexual desire). Furthermore, the more kisspeptin activated the posterior cingulate cortex—a key behavioral brain area—in response to attractive male faces, the less sexual aversion was reported by participants. Crucially, the psychometric analyses revealed that the women reported feeling "more sexy" during kisspeptin, compared to placebo.

In the second study, which was also a randomized, double-blind, two-way crossover trial, 32 heterosexual men with HSDD (aged 21–52 years) underwent a similar study with the addition of the measurement of penile rigidity, between January and September 2021.

The study demonstrated that kisspeptin significantly boosted brain activity in key structures of the sexual brain network while also increasing penile rigidity by up to 56% compared to placebo, while viewing an erotic video. Similarly to the study in women, kisspeptin also had greater effects in key <u>brain</u> regions in men more distressed with



their low sexual desire. Furthermore, psychometric analyses revealed that kisspeptin improved "happiness about sex" reported by the men.

Dr. Comninos and Professor Dhillo now plan to take this forward with larger scale studies, studies in different populations and collaborations to develop kisspeptin as a realistic treatment for both women and men with distressing psychosexual disorders.

More information: Layla Thurston et al, Effects of Kisspeptin Administration in Women With Hypoactive Sexual Desire Disorder, *JAMA Network Open* (2022). <u>DOI:</u> 10.1001/jamanetworkopen.2022.36131

Effects of Kisspeptin on Sexual Brain Processing and Penile Tumescencein Men With Hypoactive Sexual Desire Disorder, *JAMA Network Open* (2023). DOI: 10.1001/jamanetworkopen.2022.54313

Provided by Imperial College London

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