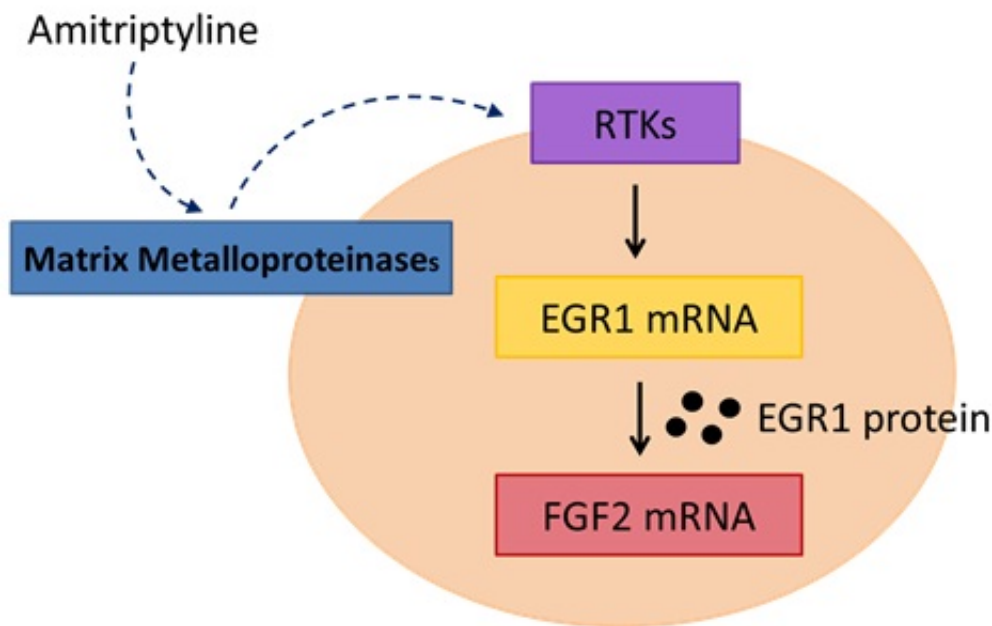


A study of antidepressants reveals how treatment helps depression management

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Treatment of primary cultured astrocytes with amitriptyline activates matrix metalloproteinases (MMPs) and receptor tyrosine kinases (RTKs, i.e., fibroblast growth factor receptor [FGFR] and epidermal growth factor receptor [EGFR]). Activated RTKs increase the mRNA and protein expression of EGR1, which in turn increases FGF2 mRNA expression. Credit: Hiroshima University

Researchers in Japan have shown that several different classes of antidepressants increase early growth responses in astrocytes, star-shaped glial cells, which could help develop new treatments.

Amitriptyline is a prototypical antidepressant that is currently used worldwide. Generally, effects of antidepressants such as [amitriptyline](#) in depressive patients become evident after treatment for a few weeks. However, no study has investigated the reasons why effects are not immediately evident.

Previous studies have shown that amitriptyline increases the mRNA expression of fibroblast [growth factor](#) 2 (FGF2) in rat astrocytes, not neurons, slowly over 24 hours. However, the cellular mechanism that leads to the expression of FGF2 following amitriptyline treatment remains unclear.

In this study, the research group treated rat primary cultured astrocytes with amitriptyline. They found that it results in the activation of [receptor tyrosine kinases](#) (RTK; fibroblast growth factor receptor [FGFR] and epidermal growth factor receptor [EGFR]), which in turn increased FGF2 mRNA expression.

Professor Yoshihiro Nakata at Hiroshima University and Dr Minoru Takebayashi at National Hospital Organization Kure Medical Center and Chugoku Cancer Center said, "activated RTK induces the phosphorylation of extracellular signal-regulated kinase 1/2 and increases EGR1 mRNA and protein expression followed by FGF2 mRNA expression."

Professor Nakata said, "the current findings expand previous findings, in that the transcription factor EGR1 could be the de novo synthesized protein that is necessary for increasing FGF2 mRNA expression evoked by amitriptyline treatment."

The amitriptyline-induced signaling cascade is essential for the [expression](#) of FGF2 mRNA in primary cultured astrocytes. This cascade could be used to guide the development of antidepressants with novel

mechanisms.

More information: "Fibroblast growth factor 2 mRNA expression evoked by amitriptyline involves extracellular signal-regulated kinase-dependent early growth response 1 production in rat primary cultured astrocytes," *Journal of Neurochemistry* 2015. [DOI: 10.1111/jnc.13247](https://doi.org/10.1111/jnc.13247)

Provided by Hiroshima University

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