# Fatty Fish May Boost Antidepressant Response

Deborah Brauser | October 22, 2014

BERLIN — Alterations in fatty acid (FA) metabolism and the way it is regulated by cortisol may be linked to response to antidepressant treatment in patients with major depressive disorder (MDD). In addition, increasing fatty fish intake may "boost" treatment response, new research suggests.

A study of 121 adults showed that those with MDD had higher adjusted levels of arachidonic acid (AA), as well as higher FA unsaturation and FA peroxidation, than their healthy peers.

**Roel Mocking**

In addition, within the MDD group, nonresponders to the selective serotonin reuptake inhibitor (SSRI) paroxetine (multiple brands) had significantly different concentrations of AA and eicosapentenoic acid (EPA)/AA than early or late responders, as well as lower levels of omega-3 docosahexanenoic acid (DHA).

However, these relationships were mediated by fish intake. The MDD group members who ate fatty fish at least once a week had a 75% increased chance of antidepressant response vs a 23% response rate for those who never ate fatty fish.

"This suggest that we could use arachidonic acids as an indicator of response, and that it might be worthwhile to target fatty acid metabolism to increase response rates to SSRIs," lead author Roel J. T. Mocking, PhD candidate from the Department of Psychiatry of the Academic Medical Center at the University of Amsterdam, the Netherlands, told *Medscape Medical News*.

"I think the take-away is that adding fatty fish offers benefits. There's no downside to recommending this to patients. It's good to eat two servings of fish a week, with one being fatty fish. And for patients [with MDD], it's like it boosts their response," said Mocking.

The study was presented here at the 27th European College of Neuropsychopharmacology (ECNP) Congress.

**First Longitudinal Analysis**

The investigators note that FA metabolism and the hypothalamic-pituitary-adrenal (HPA) axis are factors commonly thought to be involved in antidepressant response.

"These systems and their relation have been reported to be altered in [MDD]; moreover, preclinical evidence suggests an interplay with antidepressant treatment, which has not been clinically/longitudinally studied before," they add.

A total of 70 previously unmedicated patients with MDD were compared with 51 healthy peers (control group) "regarding erythrocyte membrane FAs and their relationship with salivary cortisol," report the investigators.

Those with MDD were then given paroxetine 20 mg/day for 6 weeks. The group members who did not respond to treatment at that endpoint then received 6 additional weeks of dose-escalation up to 50 mg/day. All MDD members were also divided into four subgroups on the basis of the amount of their fatty fish intake.

All participants' FA and cortisol levels were continuously measured throughout the study.

Results showed that, compared with the control group, the MDD group had higher adjusted levels of AA ($P = .002$). In addition, the MDD patients "showed more negative relationships" between FA unsaturation and FA peroxidation with cortisol than the control group.

These findings were associated with nonresponse of paroxetine treatment. In fact, nonresponders in the MDD group (n = 19) had significantly higher concentrations of AA ($P = .007$) and lower ratios of EPA/AA ($P = .02$) than both both early (n = 17) and late responders (n = 18).

The nonresponders also had significantly lower omega-3 DHA levels ($P = .02$).

**Fish Factor**

Antidepressant treatment response was also significantly associated with "time courses" of FA metabolism. FA chain length, peroxidizability, and omega-3 EPA increased in early responders (all, $P < .05$). On the other hand, nonresponders' levels started higher and decreased over time.

Intake of fatty fish mediated the relationships. Those who ate the most fish responded significantly better to antidepressant treatment than those who never ate it.

In other words, "fatty acid metabolism could be influenced by eating fish, which may be a way to improve antidepressant response rates," said Mocking.

No effect was found from treatment dose escalation on FA metabolism.

"These new data corroborate that alterations in FA-metabolism and its relationship with HPA-axis are involved in MDD-pathophysiology," write the investigators.

"Furthermore, FA-alterations and their relationship with the HPA-axis predicted antidepressant nonresponse, suggesting a modifying effect on paroxetine effectiveness," they write.

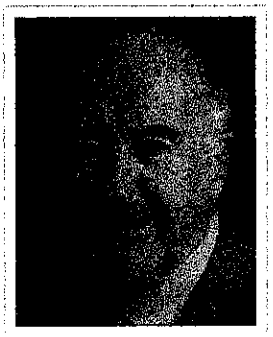
"So far, this is an association between fatty acids in blood and antidepressant response; so it's not necessarily a causal effect," said Mocking.

Still, "if we can identify factors that will predict who will or will not respond, we could eventually identify patients who would qualify for a specific treatment," he said.

He noted that the next step for the investigators is to assess whether these findings are specific for depression. "So we are currently repeating these measurements in patients with posttraumatic stress disorder and schizophrenia," he reported.

**Greater Understanding of Nonresponse**

ECNP president Guy Goodwin, FMedSci, told *Medscape Medical News* that the study findings are important.



"Understanding nonresponse to treatment with SSRIs remains an important known unknown," he said in a release.

Dr Goodwin, who was not involved with this research, is a professor of psychiatry at the University of Oxford, United Kingdom.

"There is already an intriguing association between eating fish and general health. The present study, while preliminary, takes the story into the realm of depression. Larger-scale definitive studies will be of considerable interest."

*The study authors report no relevant financial relationships.*

**Guy Goodwin**

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