NEWS

Trial sprouts doubts about broccoli extract for autism

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Broccoli boost: A compound in broccoli sprouts may counteract oxidative stress and inflammation — molecular processes implicated in autism — but some experts are skeptical.

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The newest entrant in the list of unusual autism therapies is a chemical mixture extracted from broccoli sprouts. The extract seems to improve social skills in young men with autism, a small pilot study has found[1]. But scientists caution that the study is too small to say whether the findings are reliable.

The extract is rich in sulforaphane, a compound that guards against oxidative stress, inflammation and DNA damage[2]. All of these are implicated in autism.

Sulforaphane also induces the ‘heat-shock response,’ a cellular defense mechanism against

temperature extremes[3]. Some children with autism show behavioral **improvements during bouts of fever**, which trigger the heat-shock response[4].

This led **Andrew Zimmerman**, clinical professor of pediatrics at the University of Massachusetts Medical School, to investigate whether sulforaphane eases some symptoms of autism.

Zimmerman teamed up with **Paul Talalay**, who discovered sulforaphane 25 years ago and founded **Brassica Protection Products**, a Baltimore-based company that sells products containing broccoli sprout extract.

Talalay acknowledges that sulforaphane is just one component of the extract, which contains a "huge" number of other compounds.

The team enrolled 40 males with autism aged 13 to 27 years, 26 of whom received a daily dose of the extract for 18 weeks. The remaining participants received a placebo pill. The trial was double-blind, meaning that neither the participants and their caregivers nor the researchers knew who was receiving the extract.

The people who got the extract showed improvements in various behaviors, such as interacting with others and communicating verbally, as reported by parents and clinicians. These improvements disappeared four weeks after the treatment ended. Those in the placebo group did not show any significant improvements. The results were published 13 October in the *Proceedings of the National Academy of Sciences*.

The findings hint at potential therapies for autism, but the researchers caution against drawing big conclusions. "I really want to stress to people that this study needs to be replicated to demonstrate that it's valid," Zimmerman says.

Cruciferous caution:

Some independent researchers have similar reservations, noting that the control group showed an unusually small placebo response.

"You always see a 20 to 25 percent improvement in placebo," says **John Jay Gargus**, director of the Center for Autism Research and Translation at the University of California, Irvine. For example, the placebo effect plagued **trials of the gut hormone secretin and antidepressants** for autism.

"It's stunning that they've managed to have found a placebo that doesn't give the placebo effect that we see in every other neuropsychiatric drug trial," Gargus says.

> "I really want to stress to people that this study needs to be replicated to demonstrate that it's valid."

Still, the study opens new doors in the search for autism's molecular origins, some say.

"This is an excellent exploratory study," says **Judith Miles**, emerita professor of child health at the University of Missouri, who was not involved in the study. "It exemplifies a shift to studies that identify physiological or cellular mechanisms that produce autism symptoms."

The researchers used two parent questionnaires to assess behavior: the **Aberrant Behavior Checklist**, which measures irritability, lethargy, stereotypic behavior and hyperactivity, and the **Social Responsiveness Scale**, which measures social abilities. They also used the **Clinical Global Impressions Scale** to measure autism severity.

They took baseline measurements and repeated the tests 4, 10 and 18 weeks into the trial and 4 weeks after the trial ended. By 18 weeks, nearly half of the study participants receiving broccoli sprout extract showed significant improvements in social functioning and verbal communication, as measured by the Clinical Global Impressions Scale. These are two core features of autism that are **not treated by existing medications for the disorder**.

"It doesn't change the diagnosis," Zimmerman says. "But it changes a lot of the characteristics."

Roughly 60 percent of participants in the treatment group showed improvements on the Aberrant Behavior Checklist, compared with 20 percent of those in the placebo group. About 35 percent of those in the treatment group showed improvements on the Social Responsiveness Scale, compared with none in the placebo group.

Scores on all of the tests returned to near baseline levels four weeks after the trial ended.

None of the study participants experienced adverse side effects, although those in the treatment group gained an average of 4 pounds during the 18-week trial. Two participants in the treatment group experienced seizures during or shortly after the trial. However, both had a history of seizures that they did not disclose to the researchers before the study began.

"I think that the results are really quite intriguing," says **Jeremy Veenstra-VanderWeele**, associate professor of psychiatry at Columbia University in New York, who was not involved in the study. "I love the idea of a potential treatment that causes minimal side effects."

However, he and others say they are skeptical about whether the results will hold up in other trials and in the broader population of people with autism. One concern is that 80 percent of the participants have a history of behavioral improvements during bouts of fever. Surveys estimate that roughly 30 percent of people with autism **show this 'fever effect**.' "That makes this population a little different than the typical population," Veenstra-VanderWeele says.

What's more, the improvement seen with the extract is comparable to that seen with placebo in a previous trial that involved hundreds of people with autism[5]. The benefit is probably too low to hold up in a bigger trial, says Veenstra-VanderWeele.

Still, the study findings are intriguing and warrant follow-up in a larger population, he says. "If this replicates, it's really exciting, in part because it seems very unlikely to do harm."

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