Medical Xpress

Combining medications could offer better results for ADHD patients

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Three studies to be published in the August 2016 issue of the *Journal of the American Academy of Child and Adolescent Psychiatry* (JAACAP) report that combining two standard medications could lead to greater clinical improvements for children with attention-deficit/hyperactivity disorder (ADHD) than either ADHD therapy alone.

At present, studies show that the use of several ADHD medications result in significant reductions in ADHD symptoms. However, so far there is no conclusive evidence that these standard drug treatments also improve long-term academic, social, and clinical outcomes. Research suggests that both the severity of ADHD symptoms and the degree of cognitive dysfunction that remain despite treatment contribute to poorer outcomes. As a result, more effective treatments need to be identified. One method for identifying more effective treatments is by including objective measures of the effect of ADHD treatments on brain function, which most clinical studies do not do. Using objective biological markers (or biomarkers) of patients' response to ADHD treatments could substantially advance knowledge of the neural mechanisms underlying treatment effects, helping researchers understand why there are differences in individual response.

By recruiting a sample of children and adolescents 7-14 years of age with and without ADHD, a group of researchers led by Drs. James McCracken, Sandra Loo, and Robert Bilder of the UCLA Semel Institute performed three interlocking studies examining the effects of combining standard medications on clinical, cognitive, and brain activity

measures. Combined treatment was hypothesized to be superior to the two standard medications, d-methylphenidate and guanfacine, on both clinical and cognitive outcomes, and was expected to show a distinct profile of effects on brain wave activity (EEG). Participants with ADHD were randomly assigned to eight weeks of double-blinded treatment with either d-methylphenidate, guanfacine, or a combination of the two.

Clinical results showed consistent added benefits for the combined therapy over the two single treatments, especially for symptoms of inattention, and more global response indices. The rate of good clinical response went up from 62-63% in the single drug therapy to 75% in the combined therapy.

The authors argue that the modest but consistently better treatment effects of the combined treatment may have long-term significance, as less severe symptoms may lead to better outcomes. Cognitive functioning showed a slightly different pattern. Working memory improved with both combination and stimulant treatment showing roughly equal positive effects. Guanfacine, however, showed no change in working memory function despite improvement in ADHD symptomatology. Finally, the EEG study showed that only the combination therapy resulted in improved brain activity patterns that were associated with reduced ADHD symptoms and improved cognitive functions. Taken together, the results from the three studies suggest that combination therapy resulted in the best outcomes across several different domains of function, including ADHD symptom change, working memory performance, and brain activity patterns.

"ADHD is the most commonly diagnosed neuropsychiatric disorder in children, and we know full well the risks it poses for children's future success in every area of functioning. Our current treatments clearly benefit most children in the short-term, but we've yet to find ways to protect those with ADHD from suffering many of the long-term risks,"

McCracken said. "While we are encouraged by some of the advantages we observed of the combined treatment, we have a long way to go still in improving interventions for ADHD, as seen by the more limited cognitive effects."

"These data highlight the importance of considering cognition as a major outcome," said Bilder. "In the future, we may be able to utilize multiple objective methods such as cognitive testing and EEG to individually optimize treatments, but more work is needed, including long-term studies of treatments with proven clinical and cognitive benefits." Dr. Loo added, "The use of objective biological measures in diagnosis and treatment can also help to reduce stigma, increase acceptance of the disorder, and more accurately track treatment response to yield better outcomes."

Based on these findings, the authors conclude that combining stimulants with medications like guanfacine warrants more consideration even in children with ADHD who benefit from monotherapies. Combination treatment, with appropriate monitoring, was equally well tolerated and safe in this and prior studies. Greater consideration of the cognitive effects of treatments is necessary to improve clinical outcomes. Moreover, other treatment strategies that may yield more robust benefits are needed. As technology advances, the authors hope that more objective measures of response can make their way into routine practice. Even with such improvements, the source of individual differences in ADHD treatment response remain largely unknown. Additional long-term research on the benefits of combination treatments in large samples is necessary to confirm these findings and to further advance clinical care. If validated, combined treatments of these or potentially other compounds have the potential to dramatically improve the lives of many individuals with ADHD.

More information: Sandra K. Loo et al. Effects of d-

Methylphenidate, Guanfacine, and Their Combination on Electroencephalogram Resting State Spectral Power in Attention-Deficit/Hyperactivity Disorder, *Journal of the American Academy of Child & Adolescent Psychiatry* (2016). DOI: 10.1016/j.jaac.2016.04.020

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