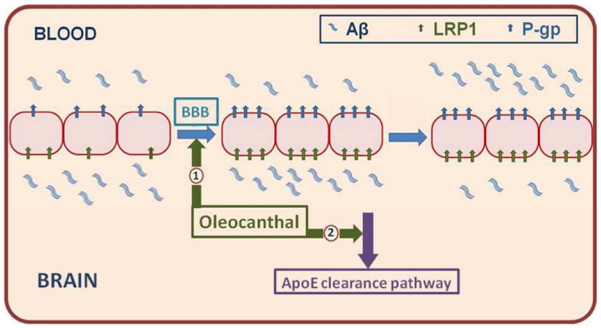
ACS Chemical Neuroscience

In This Issue

pubs.acs.org/chemneuro

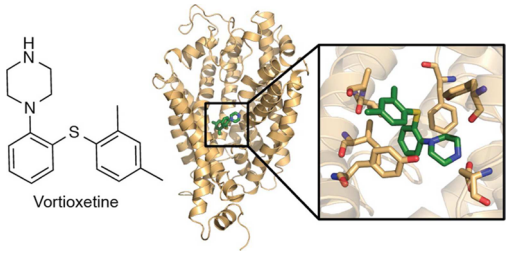
EXTRA-VIRGIN OLIVE OIL DECREASES RISK OF ALZHEIMER'S DISEASE



The phenolic component of extra-virgin olive oil, namely oleocanthal, has recently been thought to offer protection against Alzheimer's disease (AD). In the current issue, Qosa et al. (DOI: 10.1021/acschemneuro.5b00190) investigate the effect of oleocanthal treatment on different pathological markers of AD in a mouse model for AD.

The authors show that oleocanthal was able to reduce amyloid-β load in the brain as well as brain vessels. This reduced level was explained, at least in part, to the ability of oleocanthal to enhance amyloid-β clearance via upregulating amyloid-β transport proteins, LRP1 and P-gp, localized at the BBB, and by activating APOE pathway that also plays role in amyloid-β clearance. Reduced levels of amyloid-β were associated with reduced inflammatory markers in the mice brains including reduced astrocytes activation and decreased interleukin-1β levels. These results suggest oleocanthal as a novel molecule to prevent and/or treat AD.

DETAILS ON THE FUNCTIONING OF AN ANTIDEPRESSANT



The human serotonin transporter is a well-established target for the development of antidepressants. In the current issue, Andersen et al. (DOI: 10.1021/acschemneuro.5b00225) describe an interdisciplinary effort to delineate the molecular details of how a novel, multimodal antidepressant, vortioxetine (Brintellix), interacts with one of its primary targets: the human serotonin transporter.

The authors apply a comprehensive combination of chemical, biological, and computational approaches, to explain in great detail how vortioxetine binds in the central substrate (S1) binding pocket of the human serotonin transporter. This constitutes the first such study comprising a modified profile of vortioxetine compared to conventional selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac).

NEW POTENT ANALGESIC TREATS COCAINE ADDICTION

In the current issue, Varadi et al. (DOI: 10.1021/acschemneuro.5b00153) report the synthesis, in vitro binding, and in vivo analgesia of a series of 3-iodobenzoyl naltrexamine (IBNtxA) analogs. The lead compound, based on the picomolar binding affinity for kappa and delta opioid receptors was selected and further characterized in in vitro functional assays and in vivo analgesia assays. This compound was found to be a dual agonist at kappa receptors and delta opioid receptors in in vitro functional assays.

The lead compound was found to be a potent analgesic, ~15-fold higher than morphine, and this analgesia was antagonized by selective kappa and delta antagonists. The analgesia was also attenuated in kappa knockout animals confirming that kappa and delta opioid receptors mediate the analgesia in vivo. This compound showed no conditioned place preference/conditioned place aversion on its own and also blocked cocaine conditioned place preference. Unlike typical delta opioids, it showed no convulsions or seizures. Thus, dual agonists at kappa-delta receptors may be useful not only as analgesics but also as anticocaine addiction medications.

Published: November 18, 2015

DOI: 10.1021/acschemneuro.5b00290
ACS Chem. Neurosci. 2015, 6, 1780−1780