ARE WE READY NOW FOR PREVENTION TRIALS IN NON-SYMPTOMATIC INDIVIDUALS

Panos Alexopoulos, Germany

Despite the extensive clinical trials which have largely focused on therapeutics and vaccines modifying aspects of the amyloid cascade, no effective drugs against Alzheimer's disease (AD) have been developed yet. According to the prevailing interpretation, the disappointing clinical trial results could be attributed to the fact that individuals with cognitive deficits or even full-blown dementia, who suffer in fact from advanced AD pathology, have been enrolled into them. As a result, prevention studies in non-symptomatic individuals without advanced AD pathology have been proposed. There is, however, a number of arguments, which support the notion that such a strategy will prove to be ineffective too. For instance, recent reports on the pathological alterations associated with AD indicate that probably the core AD pathomechanism and its clinical implications have not been entirely unveiled or understood yet. Moreover, the clinical symptoms are not exclusively engendered by the core AD pathogenetic cascade, but by a complex interplay between brain co-pathologies including changes associated with AD, cerebrovascular alterations, Lewy bodies and harmful and protective environmental factors (e.g. cognitive reserve, exposure to occupational hazards), which significantly vary between individuals. Thus, the development of cognitive deficits cannot be easily influenced by potential pharmacological agents modifying the core AD pathomechanism. In addition, according to the diagnostic criteria for preclinical AD, its diagnosis is based on biomarkers of AD, which are markers of pathobiological processes with certain biological validity, but unclear clinical and prognostic utility. Hence, the clinical validity of the proposed criteria is still a topic of research. Furthermore, establishing the diagnosis of preclinical AD pertains to challenges (e.g. effective communication of the diagnosis, adaptation of professional practices, social policies etc) which have not been addressed yet. Last but not least, participating in drug trials is associated with potential side effects, being an important aspect for healthy individuals with still unknown risk for the development of cognitive deficits. All these arguments should be considered in the cost-benefit analysis before paving the way for prevention trials in non-symptomatic individuals.