INTRODUCTION
Alzheimer’s disease (AD) is the most common form of dementia, affecting more than 35 million people worldwide. The main risk factor is age, but genetics also play an important role, as well as having suffered a severe head trauma or severe infection in the past.

Neuroinflammation in AD is considered a consequence of neuronal degeneration by some, but also an enhancer and driving force by others. Since IL-6 is produced by microglia and astrocytes and it influences their activation, its role is crucial in the development of the disease. This paper aims to enumerate the inflammatory properties of IL-6 in the brain and to link these properties with the development of Alzheimer’s disease. As stated above, it is not clear whether neuroinflammation is a cause or a consequence of Alzheimer’s disease, in order to give a little light to it, there will be a study about the factors that make microglia and astrocytes release IL-6 and what does it provoke.

ALZHEIMER’S DISEASE
AD brains show two characteristic lesions: accumulation of β-amyloid peptides and intracellular neurofibrillary tangles. Both are found in other neurodegenerative diseases and also in healthy brains, suggesting that other factors may contribute to establish the disease. Mild cognitive impairment (MCI) is a term that includes patients who perform worst in cognitive tasks, but whom are able to live independently. The incidence of AD among MCI patients goes from 10% to 15% every year. Although amnestic MCI and mild AD patients have little cognitive differences, atrophy levels differ (Fig. 1). However, the fact that triggers the change from MCI to AD is not known.

IL-6
AD is accompanied by a rise in IL-6 levels, however it cannot be used as a biomarker because it is also increased with mere age. Both astrocytes and microglia can produce this cytokine and, at the same time, IL-6 induces their proliferation and activation and enhances the production and release of inflammatory mediators: prostaglandins, cytokines, chemokines and acute phase proteins, like APP. Moreover, IL-6 upregulates the cdk5/p35 complex which is involved in the hyperphosphorylation of Tau protein.

CONCLUSIONS
IL-6 is an inflammatory cytokine which can be produced by microglia and astrocytes in response to pathological insult, for example, as a response to Aβ. High levels of IL-6 display prominent astrogliosis and microgliosis.

When activated, neuroglia produce more inflammatory cytokines. Moreover, IL-6 induces the production of APP in microglia, which is an Aβ precursor and also activates de cdk5/p35 complex which is involved in the hyperphosphorylation of the Tau protein. Activated microglia and astrocytes show phagocytic properties and are able to remove senile plaques.

Age is seen as a state of basal inflammation enhanced by the production of proinflammatory cytokines by microglia and astrocytes which seem to be more vulnerable to activation in an advanced age. Probably, this vulnerability is increased by having suffered activations due to infection or head trauma in the past, which are known risk factors in the development of AD.

This state of basal inflammation appears to cause chronic stress to microglia and leads it to an atrophic state. Atrophic astrocytes and microglia lack of phagocytic properties and are also found in AD brains allowing the deposition of plaques (Fig 3).

Figure 1: Percentage of difference between mild AD and amnestic MCI brains. Source: Arch Neurol. 2007 October; 64(10): 1409 – 1415.

Figure 2: Progression of cognition during a lifetime. Source: National Institute on Aging (Aging)

Figure 3: IL-6 activities and its consequences in neuroinflammation and AD pathogenesis. Source: Own.