A-beta plaques that accumulate in the Alzheimer's disease (AD) brain cause cytoskeletal changes including dystrophic neurite formation. We compared the responses of pyramidal neuron (PR) and calretinin interneuron (CR) neurites associated with fibrillar A-beta plaques in human AD, APP<sub>Swe</sub>/PS1 and Tg2576 transgenic mouse models of AD. Fifty images of Thioflavine-S labelled plaques from five cases each of sporadic AD, preclinical AD (PRE) and transgenic mice were captured and over 3000 intact and dystrophic neurites per case type were analyzed. Numbers of neurofilament-labelled PR and calretinin-labelled CR neurites associated with plaques were counted and compared to age-matched human control and wild-type mouse neurites within ‘pseudo-plaques’ of similar area in analogous cortical regions. The proportion of dystrophic PR neurites traversing the Ab plaque core, edge and periphery was significantly higher than CR dystrophic neurites within all cases (p < 0.05, Dunnett’s post-hoc test). Dystrophic PR neurites constituted 40.4 ± 1.7% (SEM), 33.4 ± 1.9%, 54.6 ± 2.2% and 53.2 ± 1.7% of total PR neurites, whereas dystrophic CR neurites accounted for 9.62 ± 0.8%, 6.68 ± 0.7%, 25.62 ± 2.5% and 20.46 ± 1.7% of total CR neurites at the plaque edge in AD, PRE, APP/PS1 and Tg2576 cases respectively. We conclude that calretinin interneurons are less vulnerable to AD cytoskeletal pathology and that this resistance is conserved in relevant transgenic mouse models of AD. This apparent selective vulnerability of PR neurons in AD could be mediated by the aberrant dephosphorylation of neurofilament triplets, which are absent in CR interneurons.