Huntington's disease (HD) is the most common of a group of nine inherited neurological disorders caused by CAG triplet-repeat expansions encoding expanded polyglutamine (polyQ) sequences. They have in common the formation of aberrant intraneuronal proteinaceous inclusions bodies (IBs) containing the expanded polyQ sequences. IBs in HD and in other CAG repeat disorders are also immuno-positive for α-synuclein (α-syn), the main constituent of the Lewy bodies and dystrophic neurites characteristic of sporadic Parkinson's disease (PD) and Lewy body dementia. Point mutations in α-syn that confer a higher propensity for self-aggregation are linked to an autosomal-dominant form of PD and duplication and triplication of the α-syn gene lead to a severe and highly penetrant form of PD thus indicating that increased aggregation or levels of α-syn are sufficient to induce neurodegeneration. In view of the accumulation of α-syn in IBs in HD mice and patients and of the pathogenicity of increased α-syn aggregation or levels, we speculated that in the context of mutant Htt-induced disease, α-syn might be recruited as an additional mediator of toxicity. By isolating filamentous Htt microaggregates that form IBs of HD mice through a previously reported method, we first explore whether N-mutHtt and α-syn co-aggregate within the same filaments or whether they instead form independent microaggregates. Then, we combine the R6/1 N-mutHtt mouse model of HD with α-syn knock-out mice to elucidate whether α-syn is a relevant player in HD pathogenesis.