Altered Inflammatory signaling in Cerebrospinal Fluid (CSF) of Mild Cognitive Impairment (MCI) versus Alzheimer's disease (AD) Analysis of cytokines/chemokines, Amyloid Beta and Tau

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Introduction

- Mild cognitive impairment (MCI) is a syndrome wherein a person experiences greater cognitive decline than is normal for their age
- MCI effects 3 19% of adults aged over 65 and can progress to dementias including Alzheimer's disease (AD)
- Inflammation has been proposed as a contributor to the pathogenesis of MCI and AD
- Available data on cytokine/chemokine profile in cerebrospinal fluid (CSF) of MCI and AD patients are inconsistent

AIM: Investigate the CSF cytokine/chemokine profile of MCI and AD in comparison to healthy control donors

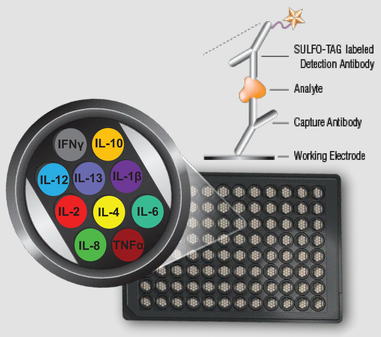
Methods

- CSF samples from MCI donors (n=15), AD donors (n=15) and aged match controls (n=15) were obtained from a biobank
- All donors completed the Mini mental state examination (MMSE)
- MCI and AD donors completed the Alzheimer's disease assessment scale cognitive (ADAS)
- A β_{1-42} and TAU (total TAU and Phospho TAU Thr181) were analysed using Meso Scale Discovery (MSD) assays
- A cytokine/chemokine panel was analysed using a MSD V Plex assay

Analytes

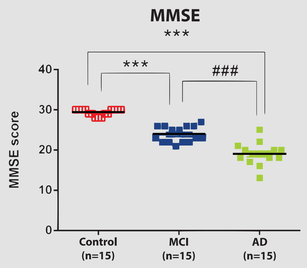
Amyloid	Proinflammatory Panel
$A\beta_{1-42}$	IL-1β
	IL-6
TAU	TNF-α
Total-TAU	IFN-γ
P-TAU (Thr181)	IL-10
	IL-12p70
	IL-13
	IL-2
	IL-8
	IL-4

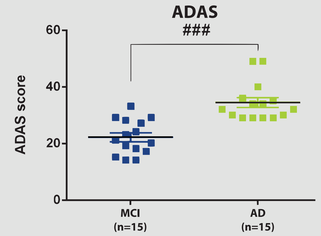
V-PLEX® MSD® Meso Scale Discovery



Results

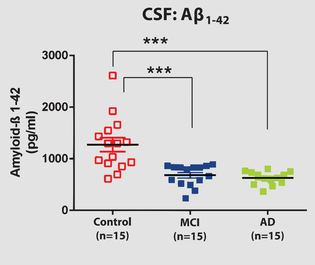
Cognitive tests: MMSE and ADAS



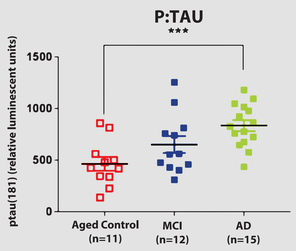


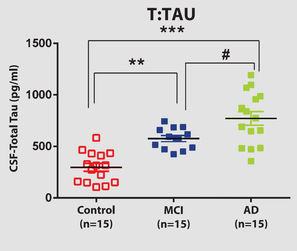
Clinical characteristics

	Control	MCI	AD
n	15	15	15
Male (n)	8	9	10
Age (mean±SD)	68 ±1.4	77 ±1.0	78 ±1.7



CSF:TAU





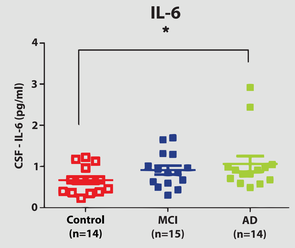
Conclusion

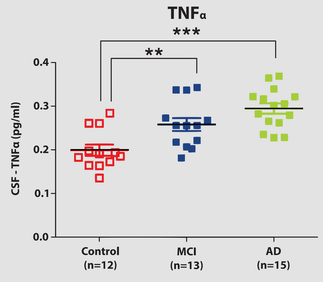
- $A\beta_{1-42}$ was decreased and T-TAU was increased in MCI and AD; P -TAU was increased in AD only
- In MCI and AD TNF α and IL -1β were increased and decreased, respectively
- Increased IL -6, IL -8 and IL -10 in AD only suggests a disease - specific cytokine/chemokine profile
- Inflammatory signalling may represent a therapeutic target and/or a biomarker of disease progression

Results

CSF: Cytokine/Chemokine expression

pg/ml	Control	MCI	AD
IFNγ	0.27 ± 0.05	0.26 ± 0.06	0.27 ± 0.03
IL-12	0.09 ± 0.01	0.07 ± 0.004	0.05 ± 0.01
IL-13	0.51 ± 0.12	0.34 ± 0.04	0.33 ± 0.03
IL-2	0.12 ± 0.01	0.17 ± 0.02	0.19 ± 0.01
IL-4	0.02 ± 0.002	0.01 ± 0.002	0.02 ± 0.002





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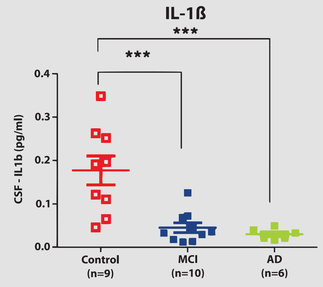

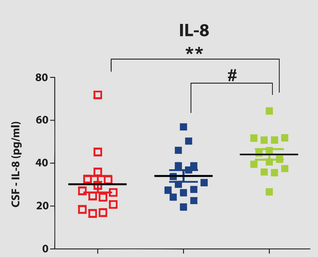

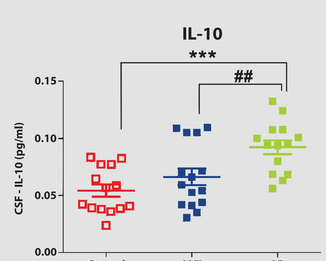

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