

Preliminary Evidence of the Impact of Intrathecal Cell Therapy with Autologous Stromal Cells on Short-Term Memory Binding in Early Alzheimer's Disease Cases

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Introduction

A decrease in brain glucose metabolism in Alzheimer's disease (AD) patients is considered a critical driver of cognitive impairment, and medications used in AD target this metabolic dysfunction. Recent evidence has shown a significant increase in glucose metabolism associated with neurocognitive improvement after intrathecal administration of bone marrow mesenchymal stromal cells (MSCs) in patients suffering from severe TBI or haemorrhagic stroke. We hypothesise that this cell therapy could also be useful in AD patients.

Participants:



- N=2
- Diagnosis of Alzheimer's disease.
- Without medication
- Detection of beta-amyloid neuritic plaques (18F-Flutemetamol-PET).
- Brain glucose metabolism studied with 18F-FDG-PET

Neuropsychological assessment:

Neuropsychological and functional assessment

Mini Mental State Examination (MMSE)	Addenbrooke's Cognitive Examination
Rey Complex Figure Test	Barthel ADL Scale
Stroop test	Lawton & Brody IADL Scale
TAVEC (Spanish adaptation to CVLT)	Clinical Dementia Rating
Wechsler Adult Intelligence Scale (WAIS-III)	

Method

Clinical procedures and experimental task:

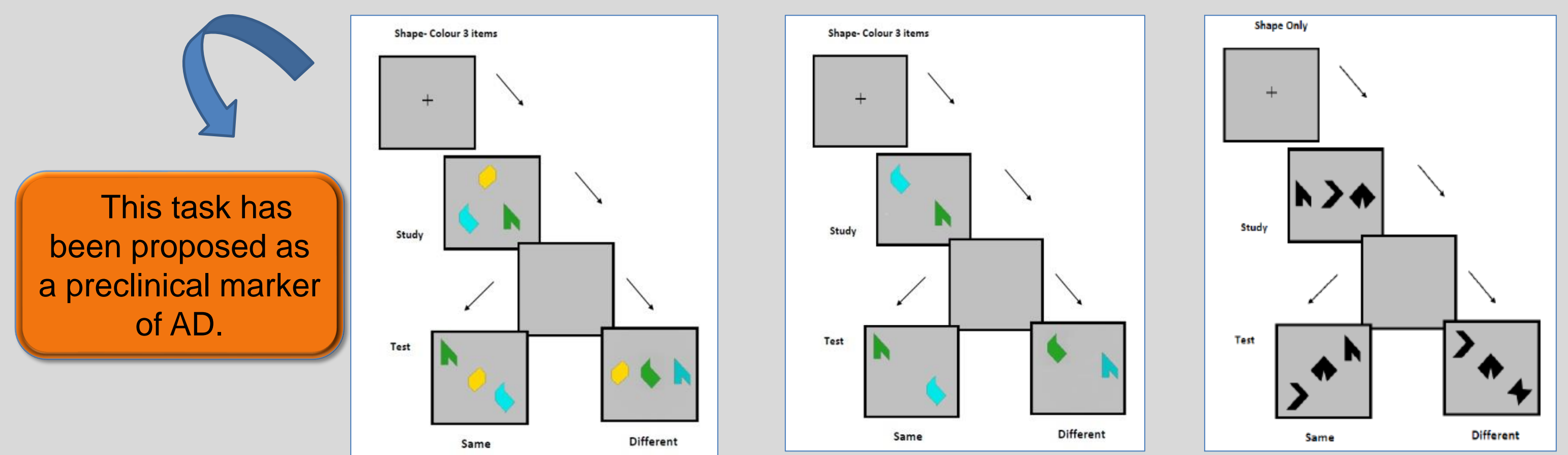
ESQUEMA PROCEDIMIENTO CÉLULAS MADRE!!!!!!:

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Image 1:

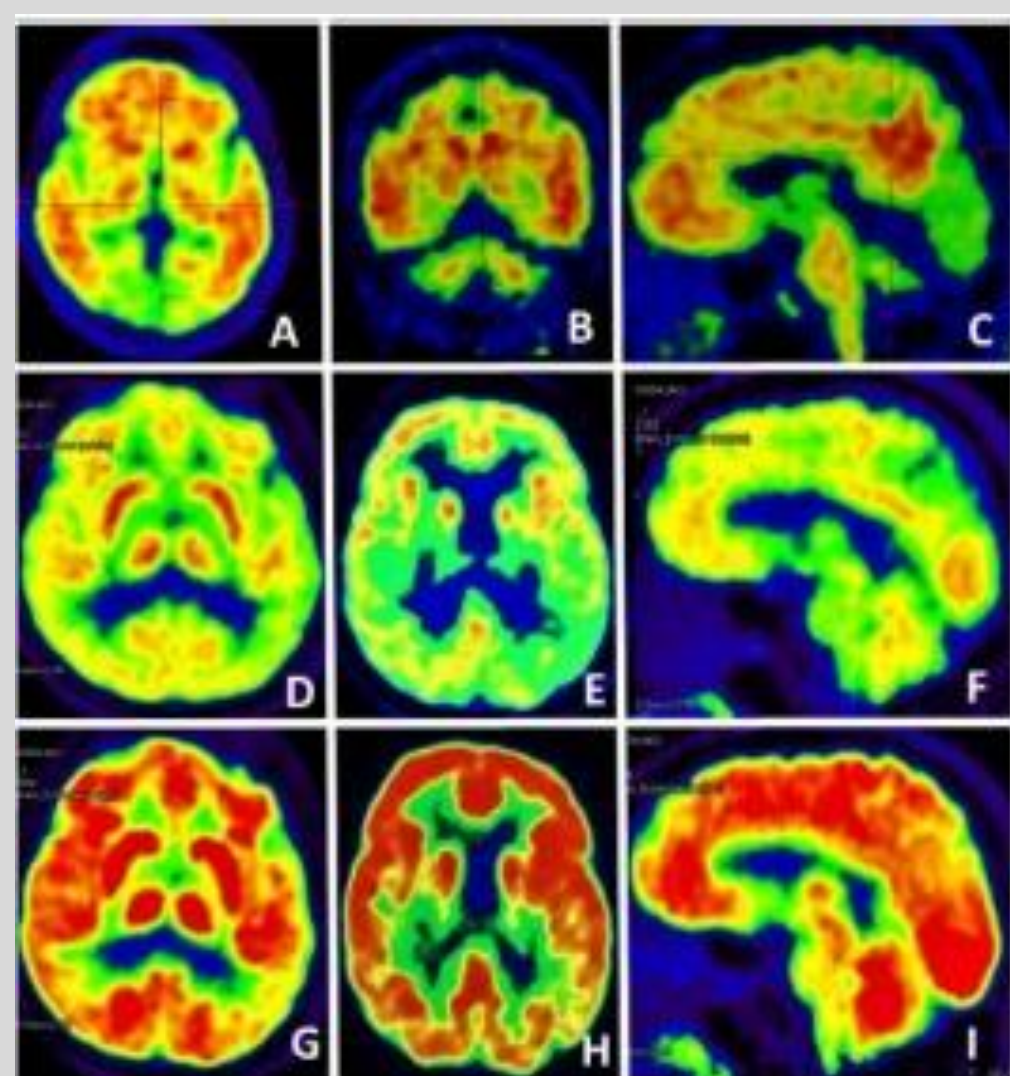
VSTMB Test: It requires subjects to detect whether or not two combinations of shape and colour change across two sequential arrays.



This task has been proposed as a preclinical marker of AD.

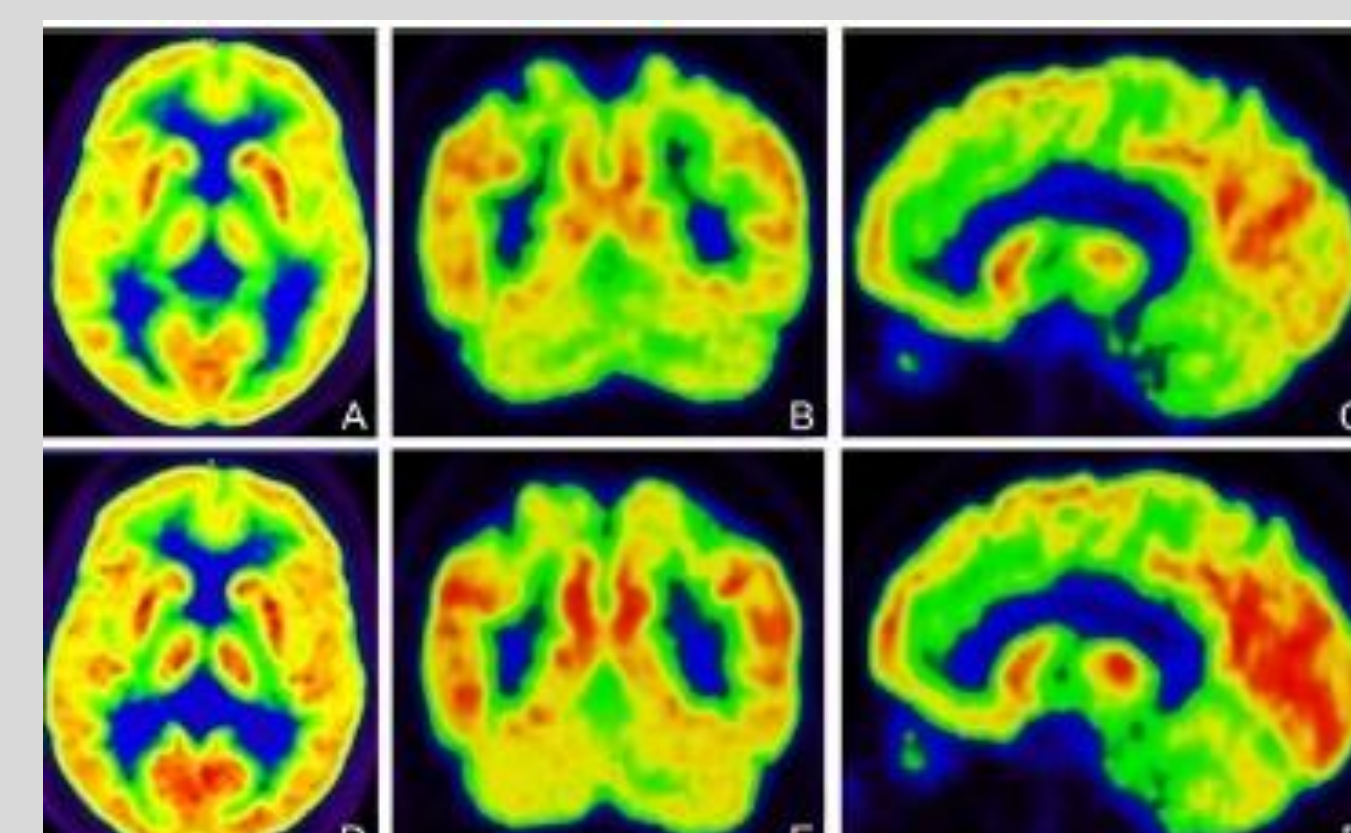
Results

Changes in 18F-FDG-PET in case 1 and case 2 from Vaquero et al, 2019.



Case 1. A-C: beta-amyloid neuritic plaques with 18F-Flutemetamol-PET.

D-E: 18F-FDG-PET previous to cell therapy and one week after first intrathecal administration of 100 millions MSCs (G-I).



Case 2. 18F-FDG-PET showing metabolic activity previous to cell therapy (A-C) and at the end of treatment (D-F).

STMB TASK	PRE	POST 1	POST 2	POST 3	POST 4	POST 5
Shape Only	100%	100%	94%	100%	100%	91%
Shape-Colour Binding	50%	62%	66%	62%	67%	81%

STMB TASK	PRE	POST 1	POST 2	POST 3
Shape Only	88%	91%	88%	88%
Shape-Colour Binding	52%	69%	66%	81%

The chance that an untreated AD patient would show more impairment than treated patients was 39.25% ($p=0.785$) for case 1, and 50.00% ($p=1.0$) for case 2. This chance increased post-treatment to 97.40% ($p=0.05$) and 99.74% ($p=0.005$) respectively.

Conclusions

Intrathecal cell therapy with autologous MSCs increases cerebral glucose metabolism, being associated with neuropsychological improvements in patients experiencing early stages of AD. This type of cell therapy is safe, allowing distribution of donor cells in the whole brain, and its utility for the treatment of AD and other diseases with cerebral impaired glucose metabolism deserves further studies. Administration of autologous MSCs should be considered as a new therapeutic strategy for Alzheimer's dementia and deserves further studies.

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