RETINAL MICROPERIMETRY: A NEW TOOL FOR IDENTIFYING TYPE 2 DIABETIC PATIENTS AT RISK OF DEVELOPING ALZHEIMER´S DISEASE

Short running title: Retinal microperimetry and cognitive impairment

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ABSTRACT

Type 2 diabetes is associated with a high risk of cognitive impairment and dementia. Therefore, strategies aimed at identifying those patients at risk of dementia are needed. Given that the retina is a brain-derived tissue it may provide a non-invasive way of examining brain pathology. The aims of the study were to evaluate whether retinal sensitivity: 1) Correlates with the specific parameters of brain imaging related to cognitive impairment; 2) Discriminates diabetic patients with mild cognitive impairment (MCI) from those with normal cognition and Alzheimer's disease (AD). For this purpose, a prospective nested case-control study including 35 type 2 diabetic patients without cognitive impairment, 35 with MCI and 35 with AD was performed. Retinal sensitivity was assessed by MAIA microperimetry and a neuropsychological evaluation was performed. Brain neurodegeneration was assessed by MRI and 18FDG-PET. A significant correlation was found between retinal sensitivity and the MRI and 18FDG-PET parameters related to brain neurodegeneration. Retinal sensitivity was related to cognitive status (normocognitive > MCI > AD; $p<0.0001$). Our results suggest that retinal sensitivity assessed by microperimetry is related to brain neurodegeneration and could be a useful biomarker for identifying type 2 diabetes patients at risk of developing AD.

INTRODUCTION

Evidence is accumulating that type 2 diabetes is associated with cognitive impairment and dementia, and numerous epidemiological studies have demonstrated that type 2 diabetic patients have a significantly higher risk (~2-fold higher) of developing Alzheimer's disease (AD) in comparison with age-matched non-diabetic subjects (1, 2). It is worth mentioning that this increased risk is maintained even after adjusting for vascular risk factors (3, 4). In addition, type 2 diabetic patients have an increase of mild cognitive impairment (MCI), which consists of cognitive impairment on standard tests but no impairment of activities of daily living and represents a transition state between normal cognitive function and dementia. The annual conversion rate from MCI to dementia ranges between 10-30% in the general population (5-7).

The number of cases of type 2 diabetic patients with cognitive impairment or dementia is expected to increase because of the diabetes pandemic and the concomitant rise in aging populations worldwide (8). In this regard, severe cognitive impairment can be envisaged as a "new" long term diabetic complication with dramatic consequences for the affected subjects and their families and with a significant impact on healthcare systems. Therefore, strategies aimed at identifying diabetic patients at risk of dementia are urgently needed.

In clinical practice there are no reported phenotypic indicators or reliable examinations to identify type 2 diabetic patients with MCI. The diagnosis of MCI is based on complex neuropsychological tests (9) which makes their incorporation into current standards of care for the type 2 diabetic population unfeasible.

In recent years, growing evidence has shown that retinal neurodegeneration is an early event in the pathogenesis of diabetic retinopathy (DR) (10, 11). The retina is ontogenically a brain-derived tissue and it has been suggested that it may provide an easily accessible and non-invasive way of examining the pathology of the brain (12, 13). Therefore, it seems reasonable to propose that the evaluation of retinal parameters related to neurodegeneration such as retinal function would be useful for identifying those type 2 diabetic patients at a higher risk of developing AD.

There are several methods for measuring retinal function. Among them, fundus-driven microperimetry has emerged as a simple, non-invasive and rapid test that can be used in the clinical practice (14, 15). Microperimetry measures retinal sensitivity in terms of the minimum light intensity that patients can perceive when spots of light stimulate specific areas of the retina. Some recent studies have suggested that microperimetry is even more sensitive than multifocal electroretinography (mfERG) in detecting early functional changes of the retina (16).

On these bases, we hypothesized that the assessment of retinal function by using microperimetry would be a useful and reliable screening test to identify type 2 diabetic patients in the early stages of cognitive impairment. Thus, this simple and rapid test would permit one to select patients in whom further evaluation in a memory clinic would be cost-effective. However, before this assumption can be accepted, it is necessary to examine whether a correlation between retinal sensitivity assessed by microperimetry and brain neurodegeneration actually exists.

The main aims of the present study were: 1) To evaluate whether retinal sensitivity assessed by microperimetry correlates with parameters of brain imaging (MRI-DTI) and function (18FDG-PET) commonly included in the diagnostic procedures of patients with cognitive impairment; 2) To determine whether retinal sensitivity assessed by microperimetry discriminates the different stages of cognitive impairment in type 2 diabetic patients (absence of cognitive impairment, MCI and AD).

RESEARCH DESIGN AND METHODS

A prospective nested case-control study (1:1:1) was designed (ClinicalTrial.gov: NCT02360527). A total of 35 patients with MCI, accomplishing the inclusion/exclusion criteria below referred to were selected from 214 consecutive type 2 diabetic patients attending a memory clinic (Fundació ACE, Barcelona, Spain). Each patient with MCI was matched with a type 2 diabetic patient with AD and a type 2 normal cognition patient by age (±4 years), diabetes duration (±4 years) and classic cardiovascular risk factors (i.e. hypertension and dyslipidemia). In addition, 20 non-diabetic subjects for each of the cognitive categories (normocognitive, MCI and AD) were included in the study as controls. The study was conducted according to the Declaration of Helsinki and was approved by the local Ethics Committee.

The main inclusion criteria were: a) Age >65years; b) Type 2 diabetes with a duration >5 years; c) Written informed consent which included accepting participation in MRI measurements, 18FDG-PET and a potential lumbar punction; d) No apparent or mild non-proliferative DR according to the International Clinical Diabetic Retinopathy Disease Severity Scale (17). The exclusion of patients with more advanced DR was based on the fact that

severe microvascular impairment could participate in neurodegeneration and the main aim of our study was to assess whether neurodegeneration of the brain and the retina runs in parallel, independently of the presence of overt microangiopathy.

The main exclusion criteria were: a) Patients with other neurodegenerative diseases of the brain or retina (i.e. glaucoma) or cerebrovascular diseases (Fazekas scale score ≤ 1) (18); b) A1c >10% (86 mmol/mol). The exclusion of patients with poor control was because very high blood glucose levels could affect retinal function (19).

All patients underwent complete neuropsychological, neurological and psychiatric evaluations as previously described (20), as well as biochemical analysis (including A1c and lipidic profile) and APOE genotyping. Brain neurodegeneration was assessed by means of MRI (for structural changes) and 18FDG-PET (for functional changes). All MRI scans were performed with a 1.5-T MRI scanner (Magnetom Symphony; Siemens Medical Solutions, Erlangen, Germany). FDG-PET measurements (mean glucose metabolism uptake) focused in the regions of interest (FDG-ROIs) which were chosen because they have frequently been reported as demonstrating hypometabolism in AD patients.

Retinal sensitivity was evaluated by fundus driven microperimetry (MAIA 3rd generation) after a previous pupillary dilation of minimum 4mm. The standard MAIA test covers a 10° diameter area with 37 measurement points and a red 1º radius circle was used as the fixation target. A 4-level fixed strategy (Goldmann III size stimulus, background luminance of 4 asb and maximum luminance of 1000 asb, with a 25 decibels (dB) dynamic range) was employed. Notably, the microperimeter automatically compensates for eye movements during

examination via a software module that tracks the eye movements. The characteristics of fixation (location and stability) were quantified and categorized according to the P1 and P2 parameters as follows: "stable" (P1 and P2>75%), "relatively unstable" (P1 <75% and P2 >75%) and unstable (both P1 and P2 <75%). The device automatically calculates the reliability index which assesses the accuracy of the test. The mean value of retinal sensitivity and reliability of the two eyes were used for data analyses.

Sample size calculation: Assuming that T2D patients present around 30% of functional retinal abnormalities (21), and considering that this figure will rise to 60% in those diabetic patients with cognitive impairment, the minimum number of patients required in each group was 25. This calculation was performed taking into account a 2-side risk level of 0.05 and a statistical power of 80%. Consequently, we considered it reasonable to extend the sample to include 35 subjects per group.

Statistical analysis

To assess differences between the groups, Chi-squared for qualitative variables and ANOVA followed by DMS post-hoc tests for quantitative variables were used. To evaluate the correlation between retinal sensitivity and MRI and 18FDG-PET variables, Spearman's correlation tests and regression analyses adjusted by age were performed. All p values were based on a two-sided test of statistical significance. Significance was accepted at the level of $p< 0.05$. The Bonferroni correction was used for multiple comparisons. Statistical analyses was performed with the SSPS statistical package.

RESULTS

The main clinical characteristics of type 2 diabetic patients included in this case-control study are shown in **Table 1**. As expected by the design, there were no differences among the groups in terms of age, diabetes duration, blood pressure or lipid profile. In addition, no differences were found regarding blood glucose control (measured by HbA1c), BMI, gender, or family history of AD.

Retinal sensitivity was lower in type 2 diabetic patients with AD in comparison with type 2 diabetic patients with MCI ($p<0.0001$). In addition, type 2 diabetic patients with MCI presented lower retinal sensitivity than age-matched patients with normal cognition ($p=0.027$) (**Table 2**). Similar results were obtained in the non-diabetic control group, but the differences between subjects with normal cognition and MCI did not reach statistical significance (Table 2). The mean of the reliability index of the microperimetry test was above 90% in all groups, thus indicating that the sensitivity measurements were accurate. Notably, a correlation ($r=-0.50$; $p<0.0001$) was found between retinal sensitivity and the Alzheimer's Disease Assessment Scale-cognition sub-scale (ADAS-Cog) in type 2 diabetic patients with cognitive impairment (**Figure 1**).

A significant reduction in the volumes of the whole brain, gray matter, hippocampus, and mean cortex was observed in AD patients in comparison with patients with MCI (**Table 3**). Regarding 18FDG-PET, a significant reduction in whole brain glucose (bilateral composite) up-take as well as a reduction in angular gyrus, cingulum and temporal glucose up-take were detected in AD patients in comparison with MCI patients **(Table 3)**.

Retinal sensitivity assessed by microperimetry was correlated with the MRI parameters commonly assessed in patients with cognitive impairment. Therefore, retinal sensitivity was directly correlated with total grey matter volume (r= 0.38; p<0.01), cortex mean thickness (r=0.37; p< 0.01), and hippocampus volume (r=0.35; p<0.01) **(Figure 2A).** In addition, retinal sensitivity correlated with whole brain glucose uptake (r=0.66; p<0.001), left angular (r=0,46; p<0.001), right angular (r=0.64; p <0.001), posterior cingulum (r=0.48; p<0.001), and temporal glucose uptake (left temporal, r=0.55; p <0.001; right temporal, r=0.32; p=0.02) in the 18FDG-PET **(Figure 2B).**

As expected, a correlation between retinal sensitivity and age was detected (r=-0.44; p<0.001). However, all the correlations above mentioned between retinal sensitivity and both MRI and 18FDG-PET parameters were maintained at significant level after adjusting for age.

Notably, when type 2 diabetic patients with MCI were analyzed separately the correlations between retinal sensitivity and 18FDG-PET parameters (whole brain glucose up-take, temporal glucose up-take and angular gyri up-take) remained at significant level.

DISCUSSION

As far as we know this is the first evidence that retinal sensitivity measured by microperimetry correlates with topography parameters of brain tissue loss (MRI) and brain hypometabolism (18FDG-PET) in type 2 diabetic patients with cognitive impairment. We found that retinal sensitivity was lower in type 2 diabetic patients with MCI in comparison with patients with normal cognition. In addition, it was lower in type 2 diabetic patients with AD compared with those with MCI. It is worth mentioning that retinal sensitivity correlated

with MRI and 18FDG-PET not only in AD but also in MCI, which can be considered a prodromal stage of AD. Notably, these correlations persisted at significant levels after adjusting for age.

Structural imaging based on MRI is an integral part of the clinical assessment of patients with suspected Alzheimer dementia. Brain atrophy is correlated with both tau deposition and neuropsychological deficits, and is a valid marker of AD and its progression (22). In our study we found a significant correlation between retinal sensitivity and total grey matter volume, cortical thickness and hippocampus volume. In this regard it should be noted that the degree of atrophy of medial temporal structures such as the hippocampus is now considered to be a valid diagnostic marker at the MCI stage (22). Therefore, our results suggest that retinal sensitivity measurements might be an adequate surrogate of MRI findings. In fact, the term "retinal sensitivity" is not appropriate because fundus-driven microperimetry not only assesses the functional status of the retina but the entire visual system and it is a dynamic test which requires short term memory, adequate perceptual speed and executive function. Interestingly, the presence of type 2 diabetic patients affects all these domains (23, 24) and, therefore, microprimetry could be a useful tool for testing all of them in an integrative manner.

Brain 18FDG-PET allows the in vivo study of cerebral glucose metabolism, reflecting neuronal and synaptic activity. While memory impairment due to AD is strictly linked to posterior cingulate and hippocampal hypometabolism, memory deficits observed during normal aging may reflect mainly a failure of encoding and the retrieval processes of episodic memory, which depends on frontal cortex integrity (25, 26). In our study, a specific correlations between retinal sensitivity and posterior cingulate and temporal gyri (which includes the hippocampus cingulum) glucose uptake were found. These findings suggest that

retinal sensitivity is a useful tool for identifying cognitive impairment related to AD, not merely age-related neuropsychological deficits.

Several structural and functional measurements of the retina have been used to indirectly examine the events that are taking place in the brain in neurodegenerative processes. Among the structural methods, optical coherence tomography (OCT), a powerful tool in the diagnosis and monitoring of diabetic macular edema, has been proposed as a method for discriminating between AD, MCI and healthy controls (27). In this regard, several meta-analysis have found a relationship between cognitive impairment and a reduction in retinal nerve fiber layer (RNFL) thickness (28-30). However, the methodology and the results were not homogeneous and the presence of diabetic patients was not taken into account in the analyses of the results. This is an important point because although retinal neurodegeneration is a hallmark of early stages of DR, glial activation or gliosis may precede the onset of neuronal death (11), thus obfuscating the detection of RNFL thinning. In addition, vascular leakage that occurs in the early stages of DR could also contribute to retinal thickness, thus also acting as a confounding factor. The new imaging methods such as angio-OCT or high-resolution technologies such as the adaptive optics scanning laser ophthalmoscope (AO-SLO) could overcome these limiting factors, but specific studies on this issue are still required.

Regarding functional methods, mfERG remains the gold standard and permits us to explore retinal function in terms of electrical response in different areas of the retina. However, this is a quite cumbersome and time-consuming examination in which corneal electrodes are necessary, and therefore it generally limited to research. By contrast, microperimetry is a simple test that requires less than 5 minutes to evaluate macular function. Microperimetry allows for exact topographic correlation between fundus details and light sensitivity

(differential light sensitivity or retinal threshold). The principle of microperimetry rests on the possibility of seeing – in real time – the retina under examination (by infrared light) and to project a defined light stimulus over an individual, selected location (31). It should be noted that microperimetry examination is independent of fixation and any other eye movement (31). Therefore, microperimetry can be recommended to ageing patients with cognitive impairment.

The American Diabetes Association recommends individualizing diabetes treatment taking into account the cognitive capacity of patients (32). Several neuropsychological questionnaires have been proposed for the screening of cognitive decline in the type 2 diabetic population (33). However, the number of patients whose cognitive function needs to be evaluated by the general practitioner or the endocrinologist/diabetologist is potentially enormous, and a more simple and cost-effective case-finding strategy to detect undiagnosed cognitive impairment is needed. Our findings reveal that retinal microperimetry can be considered an effective and reliable tool for discriminating patients with AD from those with MCI. In addition, we found that retinal sensitivity measured by microperimetry was already lower in diabetic patients with MCI when compared with diabetic age-matched subjects with nomal cognition. This is a relevant result because the identification of patients with prodromal stages of AD, such as the MCI, is precisely the target of campaigns for the early detection of AD. In addition, a relationship between retinal sensitivity measured by microperimetry and the different stages of cognitive impairment (MCI and AD) was also found in non-diabetic controls. However, in contrast with the results obtained in type 2 diabetic patients, no significant differences were found between MCI and subjects with normal cognition. This could be attributed to the higher impact of neurodegeneration in the type 2 diabetic population due to the presence of underlying mechanisms such as insulin resistance, inflammation,

oxidative stress and AGEs accumulation, which play also a key role in the pathogenesis of AD (34, 35). However, further studies with large sample sizes aimed at examining whether microperimetry could also be useful a screening test for identifying cognitive impairment in the general population are needed. Nevertheless, since diabetic patients are more prone to develop AD they represent a high risk group which should be prioritized in any programme based on a case-finding strategy in the setting of cognitive impairment. In fact, the identification of diabetic patients in the early stages of cognitive impairment is important because unrecognized cognitive dysfunction can affect treatment adherence and diabetes self-management, thus resulting in poor glycemic control, an increased frequency of severe hypoglycemic episodes, and hospital admissions (36, 37). For all these reasons, the diagnosis of cognitive impairment is not only recommendable, but can also permit us to offer a more personalized treatment for type 2 diabetic patients.

In addition, retinal microperimetry is not influenced by non-cognitive functions such as mood or depressive disorders which could influence the results of neuropsychological tests. This is an important advantage given that the prevalence of depression is two-fold higher in type 2 diabetes compared with the general population worldwide (38), and has recently been reported as being 27,5% among type 2 diabetic patients in the Mediterranean population (39). This prevalence rate could be even higher in older adults with diabetes because depressive symptoms may be overlooked (40).

In this regard, our findings point to microperimetry as a tool to be incorporated into clinical practice and in particular in any programme based on a case-finding strategy in the setting of cognitive impairment. In addition, retinal sensitivity assessed by microperimetry could be used to monitor the neuroprotective effectiveness of either antidiabetic drugs or new

treatments for preventing the development of AD. At this point, it should be noted that we have found a high correlation between cognitive impairment assessed by ADAS-Cog and retinal sensitivity. ADAS-Cog is the most widely used general cognitive measure in clinical trials of AD and has also been used as an outcome measure for trials of interventions in people with MCI (41). The ADAS-Cog consists of 11 parts and takes approximately 30 minutes to administer. Microperimetry is very rapid and depending on appropriate cost-effectiveness studies might be envisaged as a good candidate to be incorporated into current methods for monitoring the effect of neuroprotective drugs.

Our study has several limitations. First, the inclusion of some patients with only mild non-proliferative DR, HbA1c <10% (86 mmol/mol) and without cerebrovascular disease does not allow us to extrapolate the results to all the type 2 diabetic population. Therefore, a study with less strict selection criteria and with a larger sample size seems warranted. Second, the multiple statistical comparisons could have had some influence in our results but the design of the study, the "p" values obtained, and the clinical coherence of the findings makes this potential limiting factor very unlikely. Finally, although the main aim of the present study was to assess the relationship between retinal sensitivity measured by microperimetry and brain imaging in type 2 diabetic patients with MCI and AD, the obtained results should lead us to create a microperimety normative database not only of aging healthy controls, but also of type 2 diabetic subjects without cognitive impairment.

In summary, our results suggest that retinal sensitivity assessed by microperimetry is related to brain neurodegeneration and could be a useful biomarker for identifying type 2 diabetes patients at risk of developing AD.

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Table 1. Baseline characteristics of the type 2 diabetic patients included in the study.

	AD **N=35**	**MCI** **N=35**	**Normocognitive** **N=35**	**p**
Age (years)	79.55±5.66	77.02±4.88	75.71±7.04	n.s.
Gender (males, %)	42.85	51.42	57.14	n.s.
BMI (kg/m2)	27.24±3.92	28.60±4.24	29.53±3.79	n.s.
APOEε4 allele frequency (%)	42.85*	28.57	17.14*	<0.05
Hypertension (%)	80	77.14	68.57	n.s.
Dyslipidemia (%)	65.71	68.57	71.42	n.s.
A1c (% of Hb) DCCT	6.7±0.86	6.9±1.18	7.5±0.86	n.s.
A1c (mmol/mol) IFCC	49.7±0.7	51.9±10.5	58.0±0.7	n.s.
Diabetes duration (years)	11.40±6.92	13.34±9.70	12.65±6.50	n.s.
Diabetic retinopathy (%)	11.42	5.71	5.71	n.s
Diabetic nephropathy (%)	5.71	5.71	5.71	n.s.
Diabetic neuropathy (%)	2.85	2.85	2.85	n.s.
Coronary heart disease (%)	2.85	17.14	17.14	n.s.
Peripheric arteriopathy (%)	5.71	5.71	5.71	n.s.

Hypertension was defined by increased systolic (≥140mmHg) or increased diastolic (≥90mmHg) blood pressure or by the use of antihypertensive drugs. Dyslipidemia was defined by the use of lipid-lowering drugs, decreased values of HDL cholesterol (men < 0,9 mmol/L, women < 1.0 mmol/L) or by at least one increased value of total cholesterol (> 5,2mmol/L), LDL cholesterol or triglycerides (> 1.7mmol/L)

*p=0.03 between AD and normocognitive type 2 diabetic patients

Table 2.

	AD	**MCI**	**Normo-cognitive**	p
Type 2 diabetic subjects				
N	35	35	35	
Age (years)	79.55±5.66	77.02±4.88	75.71±7.04	n.s
Retinal sensitivity (dB)	17.11±6.32*	21.68±4.06*†	23.90±1.40†	<0.0001
Reliability (%)	92.57±10.92	94.88±7.16	97.66±8.97	n.s.
Non-diabetic subjects				
N	20	20	20	
Age (years)	75.25±5.56	75.10±4.76	72.15±6.65	n.s
Retinal sensitivity (dB)	16.26±6.60*	22.57±2.77*	24.23 ±0.64	<0.0001
Reliability (%)	94.59±8.66	95.19±8.76	95.84±8.97	n.s

Data were analyzed by one-way ANOVA test followed by a DMS post hoc test.

*Significant differences between AD and MCI patients after a DMS post hoc test ($p<0.0001$).

† Significant differences between MCI and normo-cognitive subjects after a DMS post hoc test ($p=0.027$).

Table 3. Imaging parameters (MRI and 18FDG-PET) of the type 2 diabetic patients with cognitive impairment included in the study

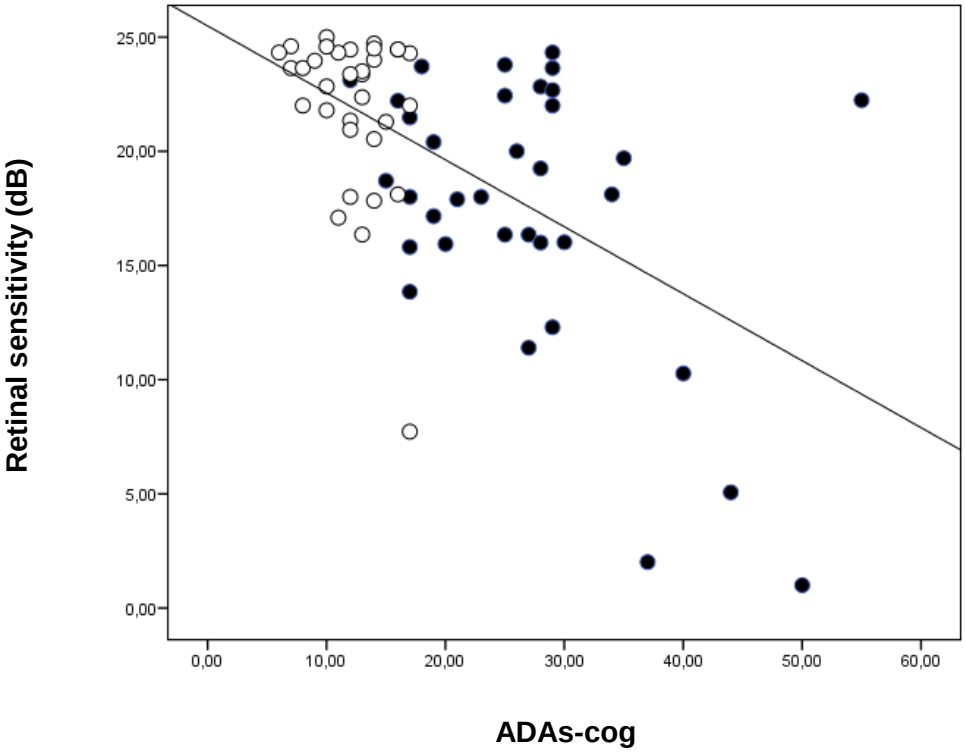
	AD **N = 35**	**MCI** **N = 35**	**p**
MRI-Total brain volume (cm^3)	938 ± 74	992 ± 101	0.002
MRI-Total grey volume (cm^3)	461 ± 43	504 ± 42	<0.001
MRI-Total hippocampus volume (cm^3)	4.92±1.03	6.11±1.10	<0.001
MRI-Cortex mean thickness (mm)	2.00±0.15	2.13±0.10	0.001
MRI-Total white matter volume (cm^3)	475±54	487±64	n.s.
MRI-White matter hypointensities (cm^3)	6.98±5.57	6.11±6.15	n.s.
FDG-ROI Left angular gyri	1.01±0.17	1.13±0.15	0.016
FDG-ROI Right angular gyri	0.99±0.20	1.16±0.08	0.001
FDG-ROI Bilateral posterior cingulate	1.20±0.10	1.35±0.13	<0.001
FDG-ROI Composite	1.04±0.13	1.19±0.09	<0.001
FDG-ROI Left temporal gyri	0.88±0.12	0.99±0.11	0.002
FDG-ROI Right temporal gyri	0.97±0.12	1.09±0.14	0.003

MRI: magnetic resonance imaging. ROI: regions of interest

FIGURE LEGENDS

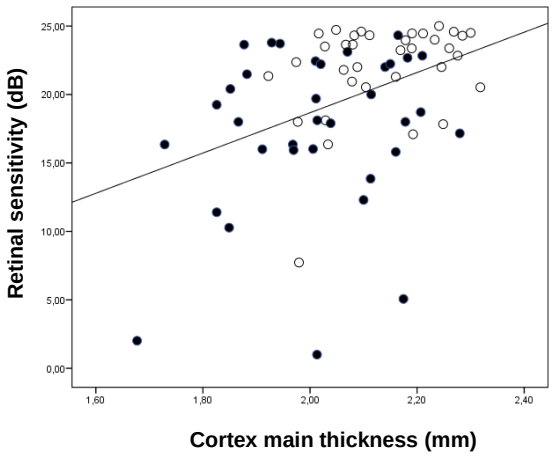
Figure 1. Correlation ($r=-0.50$; $p<0.0001$) between retinal sensitivity and ADAS-Cog. Black circles: type 2 diabetic patients with AD. White circles: type 2 diabetic patients with MCI.

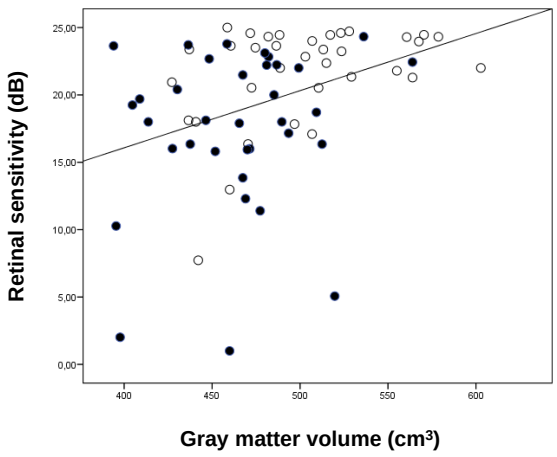
Figure 2. A) Correlation between retinal sensitivity and more representative MRI parameters (cortex main thickness, gray matter and hippocampal volume). B) Correlation between retinal sensitivity and more representative 18FDG-PET parameters (posterior cingulum, left temporal and right temporal gyri uptake). Black circles: type 2 diabetic patients with AD. White circles: type 2 diabetic patients with MCI.

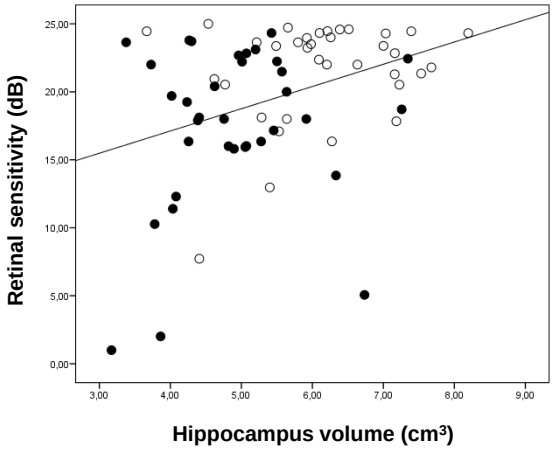

Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
0,00
10,00
20,00
30,00
40,00
50,00
60,00
ADAs-cog

Diabetes

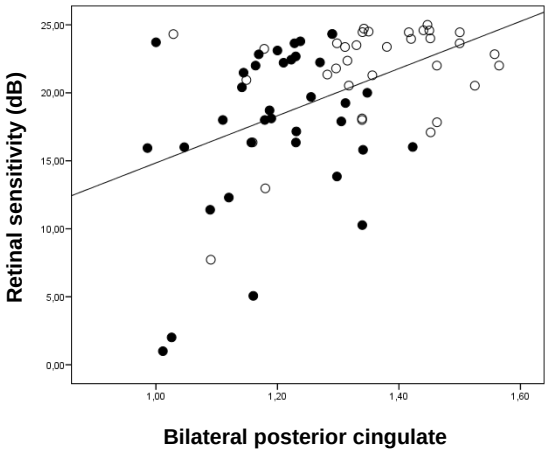
A)

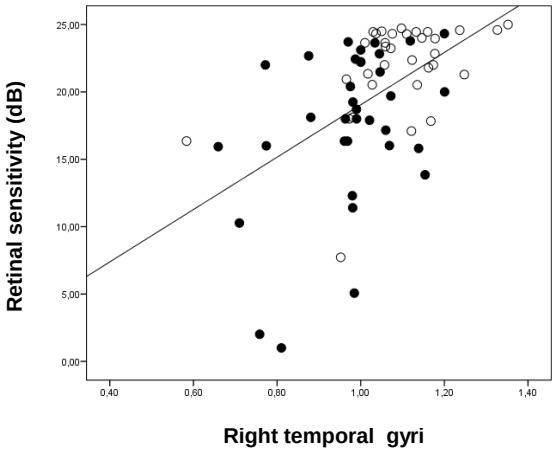

Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
1,60
1,80
2,00
2,20
2,40
Cortex main thickness (mm)

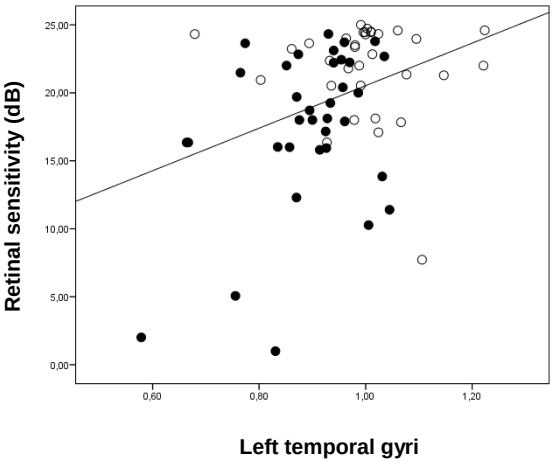

Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
400
450
500
550
600
Gray matter volume (cm³)


Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
3,00
4,00
5,00
6,00
7,00
8,00
9,00
Hippocampus volume (cm³)

B)


Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
1,00
1,20
1,40
1,60
Bilateral posterior cingulate


Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
0,40
0,60
0,80
1,00
1,20
1,40
Right temporal gyri


Retinal sensitivity (dB)
25,00
20,00
15,00
10,00
5,00
0,00
0,60
0,80
1,00
1,20
Left temporal gyri