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Relationship between Chronic Pain and Cognition in Cognitively Intact Older Persons and in Patients with Alzheimer's Disease

The Need to Control for Mood

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Key Words
Alzheimer's disease · Cognition · Executive function · Memory · Pain

Abstract
Background: Brain areas that are involved in cognition and mood also play a role in pain processing. ***Objective:*** The goal of the present study was to examine the relationship between chronic pain and cognition [executive functions (EF) and memory], while controlling for mood, in cognitively intact older persons and in patients with Alzheimer's disease (AD). ***Methods:*** Two groups of subjects participated: 20 older persons without dementia and 19 patients in an early stage of probable AD who suffered from arthrosis/arthritis. Pain intensity and pain affect were assessed by the Colored Analogue Scale for Pain Intensity and for Pain Affect, the Faces Pain Scale (FPS) and the Number of Words Chosen-Affective (NWC-A). Level of depression and anxiety were evaluated by questionnaires. EF and memory were assessed by neuropsychological tests. ***Results:*** The results show that significant correlations between specific cognitive functions, pain intensity and pain affect were lacking in the cognitively intact older persons. Cognition, in particular memory, appeared to be related to depressive symptoms. In contrast, a significant positive correlation was observed between EF, pain intensity and pain affect measured by the FPS in the AD group. ***Conclusions:*** Although older persons with depression were excluded, in studies on pain and cognition one should control for the presence of depressive symptoms in older persons with and without dementia.

Introduction

There is ample evidence, irrespective of an individual's cognitive status, that aging is associated with a high incidence of painful conditions [1]. Since age is also the major risk factor for dementia [2] and the aging society increases, it is likely that the number of dementia patients experiencing painful conditions increases as well [3].

The assessment of pain in dementia is complicated by the observation that pain experience, or a possible change in such experience, may depend on the specific subtype of dementia involved. For example, a subgroup of patients

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with Alzheimer's disease (AD) and patients with frontotemporal dementia gave indications of experiencing a decrease in the affective aspects of pain. Conversely, an increase in these aspects was observed in patients with vascular dementia [4]. These findings suggest that a possible change in pain experience depends on the specific neuropathology that is characteristic of the dementia subtype in question. A neuropathological hallmark of AD is degeneration of the hippocampus and prefrontal cortex (PFC) [5–7]. These brain areas and related neuronal circuits are involved in the processing of affective aspects of pain, cognitive-evaluative aspects of pain, pain memory and in the anticipation of affective painful stimuli [8–11]. Consequently, neuropathology in these areas and related neuronal circuits, such as the frontohippocampal circuit, may account for the decreased experience of pain observed in a subgroup of AD patients [4]. The cholinergic innervation of the hippocampus by the septum, one of the basal forebrain areas, underscores a functional relationship between the frontal lobe and the hippocampus [12]. The cholinergic neurotransmitter system is severely affected in patients with AD [12], and a recent experimental animal study showed that depletion of the cholinergic system in mice resulted in a deficit in pain memory, for example [13].

Next to pain, it is known that neuronal circuits, such as the prefrontal-hippocampal circuit, are involved in mood, e.g. depression and anxiety [14, 15]. Of note is that a relationship between depressive symptoms, anxiety and pain has been described in several studies [16–18], but has never been examined in AD patients, as far as we know.

It is noteworthy that besides pain and mood, the frontohippocampal circuit also plays a crucial role in *specific* cognitive processes like executive functions (EF) and memory [19]. A positive correlation between *global* cognitive functioning, as measured by the Mini-Mental State Examination (MMSE) [20], and anticipatory autonomic responses to pain was demonstrated in a recent study [21].

The goal of the present study was to examine the relationship between chronic pain and cognition in cognitively intact older persons and in patients with AD, while controlling for mood.

Subjects and Methods

Subjects

The sample consisted of 20 older persons without dementia (4 males and 16 females) and 19 AD patients (2 males and 17 females) in a relatively early stage, i.e. stage 5 of the Global Deterioration Scale [22], randomly selected from a sample of 500 elderly persons who live in a residential home. The age of the AD group (mean = 86.37, SD = 5.29, range 74–93 years) did not significantly differ from the age of the older persons without dementia (mean = 85.70, SD = 6.42, range 79–103 years): $t(37) = 0.35$, $p = 0.73$. Furthermore, the two groups did not differ in gender ($\chi^2 = 0.87$, d.f. = 1, $p = 0.65$).

The older persons without dementia and the AD group were screened for education (five categories: elementary school not finished: score = 1; elementary school: score = 2; lower secondary school: score = 3; higher secondary school: score = 4; higher vocational training for 18+/university: score = 5): mean = 2.74 (SD = 0.99) and 2.70 (SD = 0.73), respectively. Both groups did not differ with respect to education [$t(37) = 0.13$, $p = 0.90$].

All AD patients met the criteria of the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) for the clinical diagnosis of probable AD [23]. Subjects were excluded from participation in this study if they had vision problems, a history of psychiatric disorders, particularly depression, alcoholism, cerebral trauma, transient ischemic attack, hydrocephalus, neoplasm, epilepsy, disturbances of consciousness or focal brain disorders.

Global cognitive functioning was assessed by means of the 20-item MMSE (maximum score: 30) [20]. The MMSE evaluates orientation in time and place, registration, recall, attention and calculation, language and praxis, and visuoconstructive abilities. Considering the high mean age of the participants, an MMSE score of ≤ 23 was considered indicative for cognitive impairment [24]. As expected, the mean MMSE score of the AD group (19.63, SD = 1.77, range 17–24) and of the control group (27.30, SD = 1.95, range 24–30) differed significantly [$t(37) = 12.84$, $p < .001$]. One person in the AD group had an MMSE score of 24. However, the clinical diagnosis of the nursing home physician and the results of the neuropsychological examination justified the inclusion of that person into the AD group.

Comorbidity. The prevalence of specific categories of illness in both groups was compared to exclude the possibility of an unequal distribution of pain-inducing diseases. Specific categories of illness were heart disease, cardiovascular risk factors (hypertension and diabetes mellitus), peripheral vascular disease, lung disease, chronic renal failure, tumors, ulcers, anemia, hyper-/hypothyroidism, cholecystectomy, hearing and vision problems, urological diseases, Dupuytren's disease, migraine, diverticulosis, esophagitis, liver disturbances, psoriasis and Menière's disease. For each separate category of illness, comparisons were made between the two groups by means of χ^2 tests. Data analyses showed that there was no difference in the prevalence of specific categories of illness between both groups.

Characteristics of Painful Conditions. A prerequisite for participation in the study was that the participants had to suffer from arthrosis/arthritis of one of the joints at the lower extremity or at the lumbar spine. The medical records were kept by the former general practitioner and by the present nursing home physician. Presence of arthrosis/arthritis was determined by having the medical records reviewed by one of the authors (E.J.A.S.).

Vital and Gnostic Sensitivity. To control for possible changes in the sensory-discriminative aspects of pain, vital and gnostic sensitivity were tested. *Vital sensitivity* was tested by (1) pinprick, i.e. a needle with a blunt and a sharp side applied to the dorsal side

of both hands and to the forearms; (2) touch, assessed by touching the subject with a cotton wool and by touching the subject with one or two fingers at the same time (simultaneous extinction), and (3) temperature, assessed by applying two glass tubes filled with cold and hot water. *Gnostic sensitivity* was tested by passively moving one finger of the subject in a certain position, either bent or stretched. With closed eyes, the subject had to indicate the finger and its position. This procedure was applied to both hands. During these four tests (3 for vital sensitivity and 1 for gnostic sensitivity), the subjects were asked to close their eyes. A disturbance in each of the four conditions had a score of 1 (max. score: 4). The three separate vital sensitivity scores were summed up to form a total vital sensitivity score. Data analyses showed that the total vital sensitivity score did not differ significantly between both groups [$t(37) = 0.65$, $p = 0.52$]. Similar findings were observed for gnostic sensitivity [$t(37) = 0.07$, $p = 0.95$].

Informed Consent. The participants and their family were extensively informed about the aim and procedure of this investigation; subsequently, they gave their informed consent. A local medical ethical committee approved the study.

Methods

Assessment of Depression and Anxiety

Since depression and anxiety may show a relationship with both cognitive functioning [18] and pain [16, 17], the Beck Depression Inventory (BDI) [25] and the subscale Anxiety of the Symptom Checklist-90 (SCL-90) [26], Dutch version [27], were administered. The BDI consists of 21 questions; the score on each question ranges from 0 to 3, resulting in a maximum score of 63. The BDI can be divided into three subscales: the BDI subscale Affect (8 items: sadness, pessimism, dissatisfaction, suicidal ideas, crying, irritability, indecisiveness and weight loss), the BDI subscale Physical Function (7 items: social withdrawal, work difficulty, insomnia, fatigability, loss of appetite, somatic preoccupation and loss of libido) and the BDI subscale Self-Denigration (6 items: sense of failure, guilt, punishment, self-dislike, self-accusations and body image change) [28].

The SCL-90 is a standardized questionnaire, assessing physical and mental functioning through self-evaluation. The subscale Anxiety (10 items) has a maximum score of 50.

Assessment of Specific Cognitive Functions

Various neuropsychological tests have been administered to assess memory and EF; the administration of the tests took place only once, to avoid test-retest effects.

Memory

Digit Span Forward is a subtest of the Wechsler Memory Scale [29]. In this condition, the subjects are asked to repeat a sequence of digits (range 3–8) in the same order as read aloud by the examiner. This subtest measures short-term memory and attention, and has a maximum score of 21.

The Eight Words Test of the Amsterdam Dementia Screening test [30] was applied to assess verbal episodic memory. The *Immediate Recall* subtest consists of the total number of correct words after 5 trials (maximum score: 40). The *Delayed Recall* subtest is composed of the total number of words that are correctly reproduced after an interval of approximately 10 minutes; this subtest measures particularly active retrieval from memory store (maximum score: 8). In the *Recognition* subtest, the participant had to recognize the original 8 words from a set of 16 words. The recognition score is the total of correct responses (maximum score: 16).

Faces Recognition of the Rivermead Behavioral Memory Test [31] is a visual, nonverbal long-term episodic memory test. The test consists of a set of 10 pictures of different faces (extended version). Each card is presented in a fixed order during 4 s. After an interval of 5 min, subjects had to select the original 10 faces from a set of 20 cards. The score is the number of correct responses (maximum score: 20).

Picture Recognition of the Rivermead Behavioral Memory Test [31] measures the visual-verbal long-term episodic memory. The test consists of 20 cards (extended version) showing line drawings of various objects; each card is presented for 4 s in a fixed order. The subjects were asked to name the object on the cards. After a 5-min interval, a set of 40 cards was presented and the subjects had to select the original 20 cards. The score is the number of correct responses (maximum score: 40).

Memory Domain. The raw scores of the above-mentioned tests were transformed into z-scores and subsequently summed up to compose the memory domain (Cronbach's α: 0.86).

Executive Functions

With respect to EF, the following neuropsychological tests were included.

Digit Span Backward is another subtest of the Wechsler Memory Scale [29]. In this condition, the subjects have to repeat a sequence of digits that are read aloud by the examiner in a reversed order. Besides attention, this subtest is a measure of working memory (maximum score: 21).

In *Category Fluency*, a subtest from the Dutch Groninger Intelligence Test [32], subjects have to name as many words as possible from two different categories: animals and professions. The total score for each category is the number of correct words, produced in 60 s.

Knox's Cube Imitation Test [33] assesses visuospatial working memory. Four wooden blocks are placed in front of the subject. The examiner ticks on a number of blocks, in a predetermined order, which must be replicated by the subject. The number of blocks gradually increases. The score is the number of correct responses (maximum score: 15).

Incomplete Figures is also a subtest of the Groninger Intelligence Test [32]. The test consists of 22 incomplete figures which can only be named by using one's closure capacity. The degree of vagueness of the incomplete figures increases during the test. The score is the number of correct responses (maximum score: 20).

EF Domain. The raw scores of the above-mentioned tests were transformed into z-scores and subsequently summed up to compose the EF domain (Cronbach's α: 0.70).

Assessment of Pain Intensity and Pain Affect

To assess pain intensity and pain affect, three visual analogue scales and one pain questionnaire were administered. To increase reliability, pain assessment took place twice, with a time interval of approximately 1 month. The three visual analogue scales are described in the following.

The Colored Analogue Scale (CAS) for Assessment of Pain Intensity. The CAS is meant to assess primarily the intensity of pain in a nonverbal way [34]. The different scale positions are marked by different colors (pink at the bottom: no pain, and deep red at

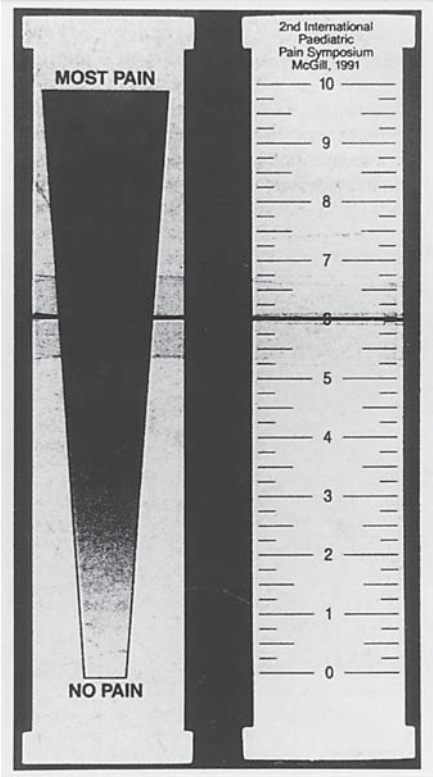

Fig. 1. CAS for the assessment of pain intensity (in cm).

the top: maximum pain) and areas which facilitate the subject's selection of a scale position which best reflects his/her pain intensity [34]. Selecting the appropriate scale position takes place by sliding a horizontal marker from the bottom to the top. The subject's score is the numerical value on the back of the scale which matches the selected scale position (range 0–100 mm; fig. 1).

CAS for Assessment of Pain Affect. The original CAS [34] was modified and used to assess the affective aspects of pain. The label 'no pain' at the bottom was replaced by the label 'no suffering' and the label 'maximum pain' at the top by the label 'a great deal of suffering'. Similar to the original CAS, each scale position referred to a number (a numerical value) which was on the back of the scale. The subject's scores ranged from 1 to 100 mm.

The Faces Pain Scale (FPS). The FPS is meant to measure both pain intensity and pain affect [35]. This scale can be reliably and validly administered to children as young as 3 years of age. Moreover, recent findings show that AD patients remain the capacity to process facial emotions [36], a prerequisite for a reliable administration of the FPS. The FPS consists of line drawings of seven faces, i.e. one neutral face and six faces which express increasing feelings of pain. Each face is 6 cm high. The faces are rank ordered from 0 to 6, from left to right. Subjects could rank their feelings from 'no pain' (score 0, the neutral face, at the extreme left side) to most severe pain (score 6, the face expressing most feelings of pain, at the extreme right side; fig. 2). The subject's score is identical to the scale number, i.e. ranging from 0 to 6.

Comprehension of the Visual Analogue Scales

Participants were tested for their comprehension of the concept. For the CAS Pain Intensity/CAS Pain Affect they were asked to move the marker to the level that reflects the most severe pain/the most suffering (top of the scale) or no pain at all/no suffering (bottom of the scale). For the FPS, they were asked to indicate which face showed the most severe pain and which face showed no pain.

The Pain Questionnaire: the Number of Words Chosen-Affective (NWC-A) of the McGill Pain Questionnaire [37] (Dutch version [38]): this affective pain scale consists of five items, with each comprising three affective adjectives. The items are arranged by increasing intensity (ranking), which allows the subjects to indicate the nature of the pain (e.g. worry or depression). The adjectives of the NWC-A were read aloud by the examiner. By adding the results of this scale, a maximum score of 15 could emerge.

Data Analyses

Since the data were not normally distributed, square root transformation was used. If both groups showed a significant difference concerning depressive symptoms and anxiety, data on cognitive function and pain experience would be analyzed by means of analyses of covariance with depressive symptoms and anxiety as covariates in both groups. Effect sizes were estimated by the partial η^2 and interpreted as: small ($\eta^2 \approx 0.01$), medium ($\eta^2 \approx 0.06$) and large ($\eta^2 > 0.13$), following Cohen's [39] standard. As only the first pain measurement took place together with the assessment of cognitive functioning and mood in AD patients and older persons without dementia, the relationship between these variables was further explored by Spearman's correlation. Only in case of a significant correlation, linear regression analysis was performed. A Bonferroni correction was applied to control for multiple comparisons, resulting in a p value of <0.005 that was considered significant. The SPSS program was used for data analyses [40].

Results

Depression and Anxiety

To provide insight into the extent depressive symptoms were present in both groups, first the mean scores, standard deviations and t tests are provided for the scores on the three subscales of the BDI and for the total BDI score. The mean scores on the BDI subscales Affect and Physical Function of the control group were significantly higher than those of the AD group. The mean score on the BDI subscale Self-Denigration did not differ between both groups.

Furthermore, the scores on the SCL-90 subscale Anxiety appeared not to differ between the AD group and the control group. For means, standard deviations and t tests, see table 1.

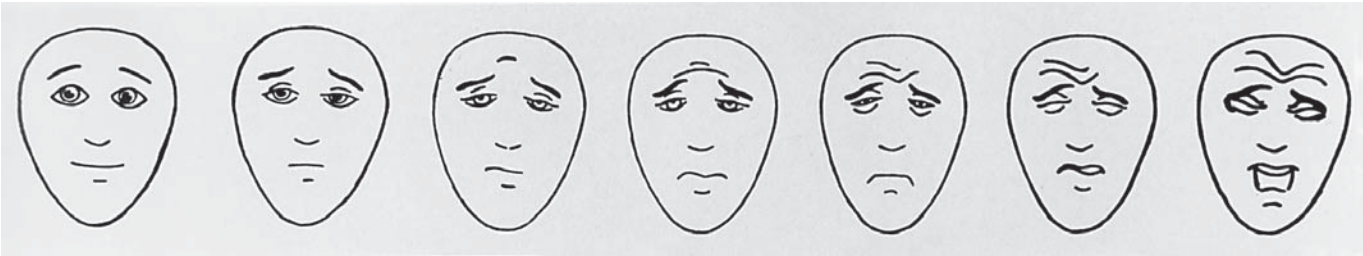

Fig. 2. FPS to measure pain intensity and pain affect.

Table 1. Means, standard deviations, and t tests concerning the scores on the three subscales of the BDI and the SCL-90 subscale Anxiety of patients with AD and older persons without dementia

Depression Anxiety	AD patients		Older persons without dementia		t tests		
	mean	SD	mean	SD	t	d.f.	p
BDI							
Affect	2.11	2.23	4.50	3.40	2.59	37	0.014
Physical Function	2.37	2.24	4.60	2.11	3.20	37	0.003
Self-Denigration	0.37	0.83	0.65	1.27	0.82	37	0.42
Total score	4.26	4.17	9.75	5.39	3.54	37	0.001
SCL-90 Anxiety	12.91	4.35	13.75	4.02	0.63	37	0.54

Cognitive Functioning

As expected, data analyses by means of univariate analysis of covariance (ANCOVA) with depressive symptoms (BDI) as covariate indicated that AD patients had a significantly lower score than older persons without dementia on the memory domain [$F(1,31) = 40.96$, $p < 0.001$]. Similarly, AD patients scored significant lower than the older persons without dementia on the EF domain [$F(1,33) = 16.26$, $p < 0.001$].

Pain Intensity and Pain Affect

First Pain Measure. An analysis of variance with depressive symptoms (BDI) as a covariate (ANCOVA) showed significantly lower scores on the CAS Pain Intensity 1, FPS 1 and NWC-A 1 in the AD patients compared to the older persons without dementia. The effect sizes were large. The means, standard deviations and ANCOVA of the scores on all four pain scales are presented in table 2.

Second Pain Measure. The extent to which patients and controls indicated to suffer from pain was in close agreement with the first moment of pain measurement (table 2). The score on CAS Pain Affect 2 was now significantly lower in the AD group compared to the older persons without dementia.

Relationships between Pain Intensity, Pain Affect, EF, Memory, Depressive Symptoms and Anxiety in Patients with AD

Data analyses by means of Spearman's correlations showed only a significant relationship between the EF domain and FPS 1 (see table 3 for Spearman's correlations and levels of significance). Based on the above-mentioned significant correlation, a linear regression analysis was performed to predict the scores on the FPS 1 from the EF domain. The standardized regression equation for predicting the FPS is:

$$\text{Predicted } Z_{\text{FPS 1}} = 0.713 Z_{\text{EF domain}}$$

Accuracy in predicting FPS 1 was high. The multiple correlation between FPS 1 and the EF domain was significant ($R^2 = 0.509$) [$F(1,15) = 15.55$, $p = 0.001$]. In other words, 51% of the variance in FPS 1 was accounted for by its linear relationship with the EF domain.

Table 2. Means, standard deviations and analyses of variance concerning the scores on the various pain scales, with the scores on the BDI as a covariate, of patients with AD and older persons without dementia

Pain scales	AD patients		Older persons without dementia		ANCOVA			
	mean	SD	mean	SD	F	d.f.	p<	η^2
CAS Pain Intensity 1	21.55	22.69	50.85	23.24	10.89	1.34	0.002	0.37
CAS Pain Intensity 2	27.00	29.67	45.89	23.36	7.77	1.34	0.009	0.19
CAS Pain Affect 1	15.79	21.34	41.20	29.01	2.14	2.36	0.132	0.11
CAS Pain Affect 2	20.89	27.17	40.83	27.59	4.77	1.34	0.036	0.12
FPS 1	0.56	0.70	2.39	1.69	10.63	1.32	0.001	0.39
FPS 2	0.79	1.05	2.33	1.45	10.43	1.27	0.003	0.28
NWC-A 1	2.00	2.69	4.42	2.67	10.92	1.34	0.002	0.23
NWC-A 2	2.35	3.64	3.78	3.00	3.98	1.33	0.054	0.11

Table 3. Spearman's correlations in the first pain measurement

	EF domain	Memory domain	CAS pain intensity	CAS pain affect	FPS	NWC-A
AD patients						
EF domain	–	–0.042	0.473	0.474	0.675**	0.129
Memory domain	–0.042	–	0.420	0.432	0.117	0.152
BDI	0.149	0.173	0.214	0.178	0.051	0.060
SCL-90 Anxiety	–0.398	–0.170	–0.060	–0.106	–0.255	0.325
Older persons without dementia						
EF domain	–	0.689**	–0.105	–0.380	–0.174	–0.336
Memory domain	0.689**	–	–0.043	–0.287	–0.428	–0.287
BDI	–0.231	–0.557*	0.203	0.342	0.410	0.401
SCL-90 Anxiety	–0.052	0.077	0.011	–0.059	0.067	0.132

* $p < 0.03$; ** $p < 0.005$.

Relationships between Pain Intensity, Pain Affect, EF, Memory, Depressive Symptoms and Anxiety in Older Persons without Dementia

Spearman's correlations showed one significant relationship: the relationship between the EF domain and the memory domain (table 3).

Discussion

Depression and Anxiety

The results show that overall (total BDI score) older persons without dementia showed more depressive symptoms than AD patients. It is justified to speak of depressive symptoms as a total BDI score of <10 is indicative for minimal depression [41]. More specifically, older persons without dementia scored higher on the BDI subscales Affect and Physical Function but not on the BDI subscale Self-Denigration. Of note is that a low score on the BDI subscale Self-Denigration is typical for chronic pain patients and not for patients with a major depression who show a high score on this BDI subscale [28]; chronic pain patients were also included in the present study.

As somatic complaints (BDI subscale Physical Function) including pain are related to anxiety in nursing home residents [42], one might have expected that the score on the SCL-90 subscale Anxiety was higher for the

older persons without dementia than for those with AD; this appeared not to be the case. One explanation emerges from animal experimental studies that show that AD neuropathology is responsible for the presence of anxiety [43]. In other words, not pain but the AD process itself may have increased the score on the SCL-90 subscale Anxiety to a level similar to that of the older persons without dementia.

Pain Experience

In agreement with the results of previous clinical studies [44–46], it was observed in the present study, irrespective of the moment of pain measurement (1 or 2), that the level of experienced pain intensity and pain affect reported by AD patients was less than the level reported by older persons without dementia. However, although in the previous studies AD patients and older persons with a depression were excluded, we did not control for the presence of depressive symptoms. Consequently, a relationship between depressive symptoms and pain within each group has not been examined in those studies. The present study did examine such a relationship which may shed a different light on previous findings, as will be addressed in the next sections.

Relationship between EF, Memory, Pain, Depressive Symptoms and Anxiety in AD

First, the lack of a correlation between EF and memory in AD patients suggests a decline in the functional relationship between the PFC and the hippocampus, respectively. A dysfunction of the hippocampal-prefrontal circuit has been observed in AD [47] and might be due to hippocampal neuropathology, which is more severe than the neuropathology of the PFC in AD [48]. Indeed, the present findings show only a significant positive relationship between EF and the FPS1, although the positive correlations between EF and CAS Pain Intensity and between memory, CAS Pain Intensity and CAS Pain Affect are also quite considerable. A significant positive relationship between EF and FPS1 implies that the better EF, the more pain intensity and pain affect the patient experiences. Of note is that the PFC plays a crucial role in EF [49], pain experience [10] and face recognition [50]. In addition, the PFC is involved in processing facial expressions of emotions [51], important for the application of the FPS. The correlations between depression, anxiety, pain intensity and pain affect were low.

Relationship between EF, Memory, Pain, Depressive Symptoms and Anxiety in Older Persons without Dementia

In the present study, a nearly significant relationship between EF and memory was observed ($p = 0.008$), supporting an active prefrontal-hippocampal neuronal circuit. Nevertheless, a significant positive relationship between EF, memory and pain experience was lacking (table 3). We argue that the depressive symptoms, which were mild but significantly higher in this group than in the AD group, were responsible for this finding. For example, a negative correlation was observed between depression and memory (rho: –0.557, $p < 0.02$), implying that the more depressive symptoms, the lower the memory performance. This suggestion has been confirmed in a recent study which observed a causal relationship between depression and cognition in community-dwelling older persons, i.e. depression may cause a decline in cognitive functioning [18]. Furthermore, positive correlations were observed between depression, CAS Pain Intensity, CAS Pain Affect, FPS 1 and NWC-A. The existence of a reciprocal relationship between pain and depression, i.e. pain may be a major cause of depression, but depression may also be a risk factor for the onset of pain, has been described in a recent study [52].

Conclusions

Results from studies that indicate that, compared to controls, AD patients suffer less from pain [44–46] should be considered with caution. The results of the present study show that although patients with depression were excluded, depressive symptoms may still be present, even more in the non-demented group. Indeed, depressive symptoms do occur in older persons without dementia, although often unrecognized [53], and may cause an increase in pain experience [17].

The high predictive value of EF for scores on the FPS 1 (reflecting pain intensity and pain affect) suggests that a neuropsychological examination might contribute to pain assessment. It is known that the PFC plays a major though not an exclusive role in EF [54]; areas such as the cerebellum and striatum are involved in EF, too [54, 55]. However, the cerebellum and striatum are also involved in the processing of painful stimuli [56, 57]. It is therefore argued that the performance on EF tasks is indicative for the functioning of neuronal circuits that also play a role in pain processing.

The present findings can only be generalized to cognitively intact older persons and AD patients with arthrosis/arthritis who do not suffer from a major depressive disorder.

Firm conclusions can only be drawn when larger groups of older persons without dementia and larger groups of patients in various stages of AD, who suffer from chronic pain, are included in future studies.

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