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Published in:
Journal of Neuropsychology

DOI:
[10.1111/jnp.12263](https://doi.org/10.1111/jnp.12263)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

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Citation for published version (APA):

Strijkert, F., Huitema, R. B., & Spikman, J. M. (2022). Measuring emotion recognition: Added value in diagnosing dementia of the Alzheimer's disease type. *Journal of Neuropsychology*, 16(2), 263-282. <https://doi.org/10.1111/jnp.12263>

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Measuring emotion recognition: Added value in diagnosing dementia of the Alzheimer's disease type

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Neuropsychological tests, particularly for episodic memory, are used to classify patients in memory clinics. Still, the differential diagnosis between dementia of the Alzheimer's disease type (Dementia-AD), mild cognitive impairment (MCI), or major depressive disorder (MDD) is challenging. However, impairments in other domains, such as emotion recognition, an aspect of social cognition, might have additional value in distinguishing Dementia-AD from MCI and MDD and hence signal progression of neurodegeneration. We evaluated this in patients visiting a memory clinic. Sixty healthy controls (HC) and 143 first time attendants of an academic hospital memory clinic who were eventually classified as Dementia-AD ($n = 45$), MCI ($n = 47$), MDD ($n = 27$), or No Impairment (NI, $n = 24$) were included. We assessed group differences in Emotion Recognition (Ekman 60 Faces Test (EFT)) and episodic memory (Dutch Rey Auditory Verbal Learning Test (RAVLT)). With multinomial and binomial regression analysis, we assessed whether EFT was added to RAVLT in distinguishing patient groups. Dementia-AD patients had significantly worse emotion recognition than HC, MCI, MDD, and NI groups, but no other between-group differences were found. Episodic memory was impaired in Dementia-AD and MCI patients. We found no memory impairments in the MDD and NI groups. Emotion recognition in addition to episodic memory was significantly better in predicting group membership than episodic memory alone. In conclusion, emotion recognition measurement had added value for differentiation between patients first visiting memory clinics, in particular in distinguishing Dementia-AD from MCI. We recommend the standard inclusion of emotion recognition testing in neuropsychological assessment in memory clinics.

Patients with neurocognitive complaints who visit a memory clinic for the first time often worry whether these complaints are early symptoms of dementia. Alzheimer's disease (AD) is the most prevalent cause of dementia (70% of patients). Mild cognitive impairment (MCI) can be a predecessor of AD: a meta-analysis performed on 41 studies, showed that annual conversion rates from MCI to AD varied from 6.8% in community samples to 8.1%

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in memory clinics (Mitchell & Shiri-Feski, 2009). However, over a ten-year period most patients did not convert to dementia. In addition, Koepsell and Monsell (2012) reported that cognitive deficits in 16% of the patients with MCI reverted to normal at a one-year follow-up.

Hence, MCI does not inevitably lead to AD, as there are many other causes and trajectories of cognitive deficits in older people. For instance, neurocognitive deficit due to depression can revert to normal after effective treatment (Muangpaisan, Petcharat, & Srinonprasert, 2012). On the other hand, depressive symptoms, for instance as manifested in major depressive disorder (MDD), may sometimes be early signs of underlying neurodegenerative disease-causing cognitive deficits (Panza et al., 2010). Hence, it is imperative to determine the exact origins of neurocognitive impairments and to disentangle confounding factors. In particular, it is important to distinguish between early AD, MCI, and MDD, since cognitive deficits in MCI and depression might be reversible or remain stable, whether or not after treatment with medication, whereas in AD, these will deteriorate over time.

Neuropsychological tests allow objective measurement of deficits in neurocognitive functions and consequently may contribute to the early prediction of future decline, stability, or reversibility (Gainotti, Quaranta, Vita, & Marra, 2014). Such tests are found to be sensitive and specific tools contributing to a diagnosis of AD, comparable with magnetic resonance imaging (MRI), and are often found to be more sensitive than fluorodeoxyglucose positron emission tomography (FDG-PET) and biomarkers like amyloid beta and tau in the cerebrospinal fluid (Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Muñoz-Ruiz et al., 2014; Schmand, Eikelenboom, Van Gool, & the Alzheimer's Disease Neuroimaging Initiative., 2011). In particular, episodic memory tests have been found to be significant predictors of progression from MCI to AD, as the hippocampus, through which episodic memories are encoded, is one of the first brain structures to deteriorate in AD (Gainotti et al., 2014). Progression from MCI to AD is usually investigated with follow-up of episodic memory tests and other neuropsychological measures after a year or more.

There is increasing acknowledgement that, in addition to memory changes, social behavioural changes can be early signs of AD as well (David, Lin, & Porsteinsson, 2016; Gallagher et al., 2011). Social behaviour is mediated by the processing of social information in order to understand others, which is known as social cognition (Adolphs, 2009; Frith & Frith, 2012). Previously, clear associations have been found between impaired social cognition and behavioural problems, such as decreased self-awareness, risky decision making, and heightened apathy in several neurological patient groups, including patients with AD, Parkinson's disease (PD), traumatic brain injury (TBI), and aneurysmal subarachnoid haemorrhage (aSAH) (Buunk et al., 2017; Spikman et al., 2013; Van den Berg et al., 2021).

Despite the fact that social cognition is put forward as one of the core components of cognitive function in the most recent edition of the American Psychiatric Association's Diagnostic and Statistical Manual for Mental Disorders (DSM-5), for clinicians assessment of social cognitive deficits is still not common practice (Henry, Von Hippel, Molenberghs, Lee, & Sachdev, 2016; Kelly, McDonald, & Frith, 2017).

A core element of social cognition is the ability to recognize emotions in facial expressions (Ekman & Friesen, 1976). Emotion recognition is associated with activity in the insula, right anterior cingulate cortex, amygdala, thalamus, and the hippocampi (Adolphs, 2002; Fusar-Poli et al., 2009). These areas are part of, or are connected to the limbic system and Papez circuit, which are in addition to emotional processing, involved

in memory functioning (Li et al., 2016; Vann & Nelson, 2015). These circuits are found to be impaired already in early stages of AD (Aggleton, Pralus, Nelson, & Hornberger, 2016; Li et al., 2016). However, there are indications that the limbic system and Papez circuit are affected in patients with depression as well, which can result in emotional dysregulation (Jiang et al., 2015). Consequently, it seems relevant to investigate emotional processing in patient groups visiting the memory clinic.

In recent years, studies investigating emotion recognition in patients with AD, MCI, and MDD showed mixed results. Several studies found impaired emotion recognition in AD patients compared with healthy older adults (Klein-Koerkamp, Beaudoin, Baciú, & Hot, 2012; Sapey-Triomphe et al., 2015), whereas others found no differences (Bucks & Radford, 2004; Burnham & Hogervorst, 2002). For MCI patients as well, some studies reported deficits in emotion recognition compared with healthy older adults (Fujie et al., 2008; Spoletini et al., 2008), while others reported no deficits at all or different findings for patients with single domain MCI versus multiple domain MCI (Bediou et al., 2012; Teng, Lu, & Cummings, 2007; Weiss et al., 2008). Emotion recognition in MCI patients compared with AD patients results in even more diverging findings, with comparable performances reported, as well as greater impairment in AD (Bediou et al., 2012; Spoletini et al., 2008). Finally, patients with MDD and other mood disorders were found to have overall worse facial emotion recognition than healthy adults (Dalili, Penton-Voak, Harmer, & Munafó, 2015; Kohler, Hoffman, Eastman, Healey, & Moberg, 2011), but better performances than patients with AD (Phillips, Scott, Henry, Mowat, & Bell, 2010). Overall, deficits in general cognition were associated with impairments in emotion recognition in these patient groups, but after controlling for general cognition, AD patients remained impaired in emotion recognition, compared with healthy controls, suggesting specific emotion recognition deficit (Klein-Koerkamp et al., 2012; Phillips et al., 2010).

Regarding specific emotions, more divergent findings have been reported, although findings have in common that impairments concern the recognition of any of the negative emotions anger, disgust, fear, and sadness (NER; Negative Emotion Recognition). In several studies, AD patients were mainly impaired in recognizing fear and sadness, whereas the recognition of disgust was relatively preserved (Henry et al., 2008; Phillips et al., 2010; Sapey-Triomphe et al., 2015). However, in another study the recognition of disgust was impaired in AD patients, but preserved in MCI patients (Bediou et al., 2009). Specific impairments in NER were found to be associated with an increase in social behavioural problems in patients with acquired brain injury (ABI), as reported by informal caregivers (Jorna et al., 2021). Regarding MDD, in one meta-analysis impaired recognition of the emotions anger, disgust, fear, happiness, and surprise was reported and no impairments in sadness (Dalili et al., 2015). In contrast, in a second meta-analysis a more general emotion recognition deficit was reported in patients with mood disorder, but no specific deficits in (negative) emotions (Kohler et al., 2011). The authors of both meta-analyses report low statistical power due to small sample sizes of the included studies.

To summarize, there are indications that emotion recognition may be affected in patients who visit a memory clinic, be it AD, MCI, or MDD, but findings up to now have been controversial and discrepancies not thoroughly investigated. Furthermore, until now there have been no studies that directly compared emotion recognition in these different patient groups and investigated to which extent measurement of emotion recognition contributes to differentiating between these patient groups. Therefore, the aim of the present study is to investigate to which extent deficits in emotion recognition are present in different patient groups visiting the memory clinic and in particular

whether a test of emotion recognition has added diagnostic value in discerning different diagnostic patient groups.

Methods

Participants

Patients were included as part of an ongoing research trial (the Parelsnoer Initiative for Neurodegenerative Diseases, a Dutch national biomarker databank), for which they gave informed consent, as well as through database investigation of the memory clinic. Both were in accordance with the Helsinki Declaration, and the research was approved by the ethics committee of the university hospital. Data were handled anonymously. Patients were selected from all patients who visited the memory clinic and underwent expert neurological and psychiatric screening, as well as a neuropsychological examination, which included at least two tests per cognitive domain. Diagnoses were confirmed after consensus was reached by an expert panel consisting of a neurologist, psychiatrist, radiologist, and neuropsychologist.

A total of 143 patients were included in this study (age range: 47–87 years) according to the following criteria:

- Dementia of the Alzheimer's disease type, (Dementia-AD; National Institute on Aging-Alzheimer's Association diagnostic guidelines, NIA-AA) (McKhann et al., 2011).
- Amnesic mild cognitive impairment (aMCI; Petersen/Winblad criteria) (Petersen et al., 1999).
- Major depressive disorder (MDD; DSM-IV-TR criteria; American Psychiatric Association, 2000)
- Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) assessing general cognition was equal to, or higher than, 20 points (maximum 30 points).
- Clinical Dementia Rating Score (CDR) was not higher than 1 (mild dementia) (Morris, 1993).
- A fourth category labelled 'No Impairment' (NI) was comprised of patients who were referred to the memory clinic with cognitive complaints, but for whom after extensive examination, no diagnosis (Dementia-AD, MCI, or MDD) was given.

Furthermore, 60 healthy control participants (HC) were recruited in a similar age range as the patients (51–89 years). Most of the HCs were partners of patients, who were asked to participate in the current study during the diagnostic partner interview of the memory clinic. HCs had to give informed consent and were included if they did not report cognitive complaints, their MMSE score was equal to, or higher than, 28, and CDR was zero (no dementia or MCI). Exclusion criteria were as follows: previous history of serious neurological or psychiatric disorders, recent hospitalization including narcosis/reanimation, substance abuse, or use of medication that could impact cognition. Healthy controls that were partners of patients did not display heightened anxiety or depressive symptoms, as measured with the Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith, 1983). Level of education was measured on a 7-point scale (ranging from less than six years of formal education (level 1), to academic level (level 7)), based on the Dutch Verhage scale (Verhage, 1964). In the current study, participants with educational level 1 ($n = 2$) were excluded.

Measures

Emotion recognition

Emotion recognition was assessed with the Ekman 60 Faces Test (EFT), part of the FEEST: Facial Expression of Emotions-Stimuli and Tests (Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002). The EFT contains 60 photographs of faces depicting six basic emotions: Anger, Disgust, Fear, Happiness, Sadness, and Surprise (ten of each). Participants choose which of the six emotions best fits the faces presented in the photographs. Eight AD patients performed the computerised version of the EFT. All other patients and HCs ($N = 195$) performed a booklet version. In both versions, a practice session was undertaken. For the booklet version, stimulus presentation was in a fixed order. In the computerised version, stimuli were presented at random. In both the booklet and the computerized version, patients were presented with verbal labels of the six emotions and gave verbal responses. The test leader transcribed this on a test form in the booklet version or clicked on the label presented on the computer screen in the computerized version. Lighting conditions and distance from the stimuli were similar. In the booklet version, participants were encouraged to provide a speedy answer, but there was no time limitation on stimulus or response presentation. In the computerized version, there was a limit on stimulus presentation (5 s per stimulus), but not on response presentation. Non-parametric Mann–Whitney tests indicated that there were no significant differences in mean EFT performances between AD patients that were exposed to either the booklet or computerised version (EFT-Total: $U = 133.5$, $z = -.43$, $p = .67$).

Total score range for EFT-Total is 0 to 60. The range for EFT-Anger, EFT-Disgust, EFT-Fear, EFT-Happiness, EFT-Sadness, and EFT-Surprise is 0–10. Furthermore, a NER score is computed by adding the scores on EFT-Anger, EFT-Disgust, EFT-Fear, and EFT-Sadness, for which the range is 0–40.

Memory performance

The Dutch version of the Rey Auditory Verbal Learning Test (RAVLT) (Saan & Deelman, 2012), measures verbal (episodic) memory. This includes an immediate recall score (RAVLT-IR), based on the sum of five subsequent immediate recall trials (score per trial: 0–15), resulting in a total score range from 0 to 75. A delayed recall score (RAVLT-DR) was also determined, based on the number of words retrieved 20 min after RAVLT-IR (range: 0–15). The RAVLT was part of the neuropsychological examination of which the results were used to establish a diagnosis. However, this was not the only memory measure: at least one and often two visual memory tests were included to establish possible memory deficits.

Data analysis

Statistical Package for the Social Sciences (IBM SPSS Statistics 23) was used with level of significance set at $\alpha < .05$. Differences in age and level of education between the groups were assessed with univariate ANOVAs, and in sex with a chi-square test, with 'group membership' (i.e. Dementia-AD, MCI, MDD, NI, and HC) as independent variable. Demographic characteristics were added as covariates in subsequent analyses. ANCOVAs were performed to assess possible differences in the EFT-Total, EFT-Subscores (EFT-Anger, EFT-Disgust, EFT-Fear, EFT-Happiness, EFT-Sadness, and EFT-Surprise), MMSE and the memory scores (RAVLT-IR and RAVLT-DR) between all groups, including post hoc

pairwise comparisons (including Dunn–Sidak corrections for multiple comparisons) using the estimated marginal means.

Prior to a multinomial regression analysis, partial correlations (controlled for demographic characteristics) were computed for the entire group of patients (HC group excluded due to lack of range in MMSE scores) between MMSE, RAVLT-IR, RAVLT-DR, and EFT-Total, in order to assess whether these variables were (relatively) independent from each other. To assess a possible relationship between general cognition and emotion recognition, partial correlations were computed between MMSE and EFT-Total, for every separate diagnostic category (HC group excluded).

To address the question whether the EFT adds value to distinguishing patient groups visiting the memory clinic from each other, we performed a multinomial logistic regression analysis with group membership (i.e. HC, NI, MDD, MCI and Dementia-AD) as dependent variable and Age, RAVLT-IR, and EFT-Total as predictor variables. We used a forward stepwise procedure in which the aforementioned predictors are added in order of the size of the decrease in unexplained variance in the model; only significant predictors are added. The HC group served as the reference category. To assess the decrease in unexplained variance by adding the predictors, chi-square test statistics, odds ratios, and 95% confidence intervals were reported. To assess whether, in addition to the RAVLT, the EFT has significant value in differentiating between Dementia-AD and MCI, a binomial logistic regression analysis was performed with group membership (only Dementia-AD and MCI) as dependent variable and RAVLT-IR and EFT-Total as predictor variables. Effect sizes were reported. Additionally, the multinomial logistic regression analysis was repeated with RAVLT-IR and the NER score as predictor variables.

Results

Demographic characteristics

Table 1 shows a significant difference between the groups on Age, but not on Sex and Education. The Dementia-AD group was significantly older than the MDD group ($p < .01$).

Emotion recognition

Table 2 shows that overall, significant differences between the groups were found for EFT-Total, as well as for EFT-Disgust, EFT-Fear, EFT-Happiness, and EFT-Sadness. Overall, differences for EFT-Surprise and EFT-Anger were not significant. Results of the post hoc pairwise comparisons for EFT-Total, as well as the six separate basic emotions, are represented in Figure 1a–g.

General cognition and memory performance

Table 3 shows significant overall group differences for MMSE, RAVLT-IR, and RAVLT-DR. In post hoc pairwise comparisons, the Dementia-AD group had significantly lower MMSE scores than all other groups ($p < .01$). The MCI group and the MDD group had significantly lower MMSE scores than the HC group (both $p < .01$). Furthermore, no significant differences were found between Dementia-AD and MCI groups on RAVLT-IR and RAVLT-DR; however, both groups had significantly lower scores on RAVLT-IR and RAVLT-DR compared with the MDD, NI, and HC groups (all $p < .01$). Finally, the MDD, NI, and HC groups did not differ significantly from each other on both RAVLT-IR and RAVLT-

Table 1. Demographic characteristics and statistical test results (ANOVA for Age and education and chi-square for Sex) for the HC, NI, MDD, MCI, and Dementia-AD groups

	HC (n = 60)	NI (n = 24)	MDD (n = 27)	MCI (N = 47)	Dementia-AD (N = 45)		
Age in years (M & SE) Range	66.9 (1.4) 51–89	66.3 (2.0) 49–82	63.3 (1.5) 47–75	67.5 (1.2) 52–83	71.6 (1.2) 51–87	F(4,198) = 3.76	p < .01
Education (M & SE) Range	5.1 (0.1) 2–7	5.4 (0.3) 3–7	5.2 (0.2) 4–7	5.3 (0.2) 3–7	4.8 (0.2) 2–7	F(4,198) = 0.97	p = .43
Sex (F/M)	32/28	6/18	10/17	20/27	22/23	chi ² = 6.63	p = .16

Note. Means (M) and Standard Errors (SE) are shown, except for Sex (ratio).

HC = Healthy Control, NI = No Impairment, MDD = Major Depressive Disorder, MCI = Mild Cognitive Impairment, Dementia-AD = Dementia of the Alzheimer's Disease Type.

Table 2. Emotion recognition in the HC, NI, MDD, MCI, and Dementia-AD groups, measured with Ekman 60 Faces Test (EFT). Displayed are means, standard errors, and test statistics (*F*, *df*) for ANCOVA with Age, Sex, and Education as covariates

	HC (<i>n</i> = 60) <i>M</i> (<i>SE</i>)	NI (<i>n</i> = 24) <i>M</i> (<i>SE</i>)	MDD (<i>n</i> = 27) <i>M</i> (<i>SE</i>)	MCI (<i>n</i> = 47) <i>M</i> (<i>SE</i>)	Dementia-AD (<i>n</i> = 45) <i>M</i> (<i>SE</i>)	<i>F</i> (<i>df</i>)	Sig.
EFT-Total	48.3 (0.8)	48.5 (0.9)	48.7 (1.1)	46.4 (0.9)	41.7 (1.2)	<i>F</i> (4,195) = 6.74	<i>p</i> < .01
EFT-Anger	7.5 (0.2)	7.7 (0.3)	7.6 (0.3)	7.5 (0.3)	6.7 (0.4)	<i>F</i> (4,195) = .66	<i>p</i> = .62
EFT-Disgust	8.1 (0.3)	8.6 (0.3)	7.8 (0.3)	7.7 (0.3)	6.9 (0.4)	<i>F</i> (4,195) = 4.36	<i>p</i> < .01
EFT-Fear	6.6 (0.3)	6.6 (0.4)	6.9 (0.5)	5.5 (0.4)	4.5 (0.3)	<i>F</i> (4,195) = 4.26	<i>p</i> < .01
EFT-Happiness	9.9 (0.0)	9.8 (0.1)	9.9 (0.1)	10.0 (0.0)	9.6 (0.1)	<i>F</i> (4,195) = 3.56	<i>p</i> < .01
EFT-Sadness	7.3 (0.2)	7.1 (0.3)	7.4 (0.3)	6.8 (0.3)	5.7 (0.3)	<i>F</i> (4,195) = 3.07	<i>p</i> = .02
EFT-Surprise	8.9 (0.2)	8.7 (0.3)	9.1 (0.2)	9.0 (0.2)	8.2 (0.3)	<i>F</i> (4,195) = 2.23	<i>p</i> = .07

Note. EFT-Total= Ekman 60 Faces Test Total Score. Uncorrected Means (*M*) and Standard Errors (*SE*) are shown.

HC = Healthy Control, NI = No Impairment, MDD = Major Depressive Disorder, MCI = Mild Cognitive Impairment, Dementia-AD = Dementia of the Alzheimer's Disease Type.

DR. For MMSE, covariates Education ($p < .01$) and Sex ($p = .04$) were significant. All covariates were significant for RAVLT-IR (Age and Sex $p < .01$, Education $p = .04$), for RAVLT-DR only Age was a significant covariate ($p < .01$).

Correlations between emotion recognition, general cognition, and memory performance

After correcting for multiple comparisons, significant positive but small partial correlations (controlled for Age, Education, and Sex) were found in the entire group (HCs excluded) between both RAVLT-IR and EFT-Total ($r = .27, p < .01$), and RAVLT-DR and EFT-Total ($r = .24, p < .01$). A significant positive correlation with medium effect size was found between MMSE and EFT-Total ($r = .33, p < .01$). Between MMSE and RAVLT-IR ($r = .59, p < .01$) and MMSE and RAVLT-DR ($r = .51, p < .01$), we also found significant positive correlations, with large effect sizes. Correlations between RAVLT-IR and RAVLT-DR were large ($r = .86, p < .01$). The reported correlations with large effect sizes reflect that there is too much overlap between MMSE and EFT, MMSE and RAVLT-IR and RAVLT-DR, as well as between RAVLT-IR and RAVLT-DR. Therefore, MMSE and RAVLT-DR were not added as independent predictors to the regression analysis.

For the separate diagnostic categories, after correcting for multiple comparisons, we found partial correlations (controlled for Age, Education, and Sex) with large to medium effect size between MMSE and EFT-Total in the MDD and MCI groups (respectively $r = .53, p = .01$ and $r = .37, p = .03$), which were non-significant after correcting for multiple comparisons. In the NI and Dementia-AD groups, we found non-significant partial correlations with small effect sizes between MMSE and EFT-Total (respectively $r = -.03, p = .89$ and $r = .16, p = .37$).

Predictions of group membership

In the multinomial logistic regression analysis predicting group membership (i.e. HC, NI, MDD, MCI, and Dementia-AD), the HC group served as reference category and predictors Age, RAVLT-IR, and EFT-Total were added in a forward stepwise procedure (see Methods section). The likelihood ratio tests showed that Age did not have a significant contribution (decrease unexplained variance) to the final model ($\chi^2 = 3.35, p = .50$). Hence, Age was automatically not added in the stepwise procedure. RAVLT-IR (Model 1: $\chi^2 = 94.10$,

Figure 1. (a–g): Emotion recognition in the HC, NI, MDD, MCI, and Dementia-AD groups as measured with Ekman 60 Faces Test (EFT). (a): Total emotion recognition as measured with Ekman 60 Faces Test (EFT-Total, range: 0–60). (b): Recognition of anger as measured with Ekman 60 Faces Test (EFT-Anger, range: 0–10). (c): Recognition of disgust as measured with Ekman 60 Faces Test (EFT-Disgust, range: 0–10). (d): Recognition of fear as measured with Ekman 60 Faces Test (EFT-Fear, range: 0–10). (e): Recognition of happiness as measured with Ekman 60 Faces Test (EFT-Happiness, range: 0–10). (f): Recognition of sadness as measured with Ekman 60 Faces Test (EFT-Sadness, range: 0–10). (g): Recognition of surprise as measured with Ekman 60 Faces Test (EFT-Surprise, range: 0–10). Bars represent the following groups: HC = Healthy Controls; NI = No Impairment; MDD = Major Depressive Disorder; MCI = Mild Cognitive Impairment, Dementia-AD = Dementia of the Alzheimer’s Disease Type. Error bars show standard errors. * represent significant differences between groups at alpha level $p < .05$. ** represent significant differences between groups at alpha level $p < .01$.

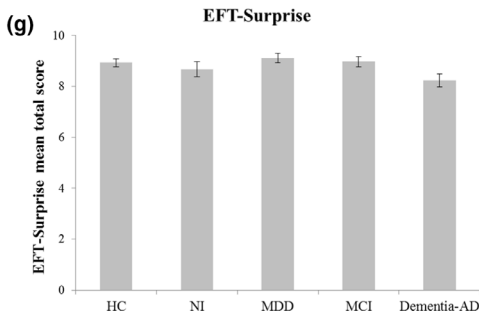
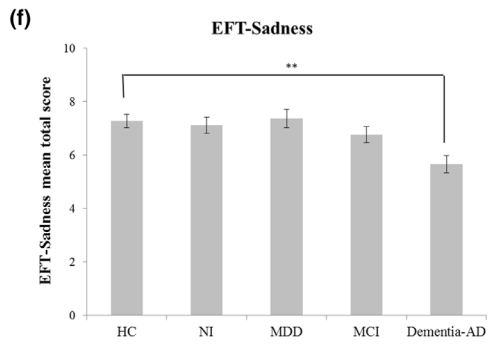
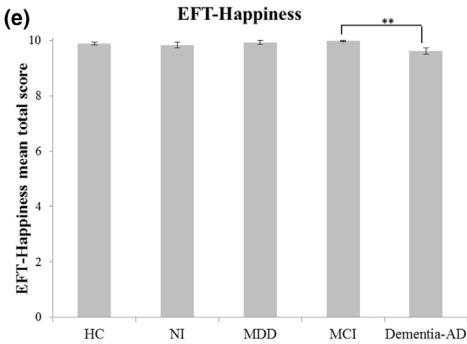
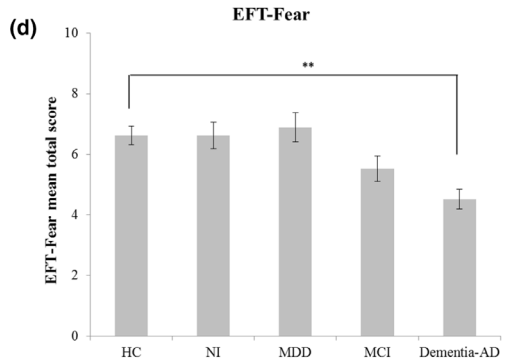
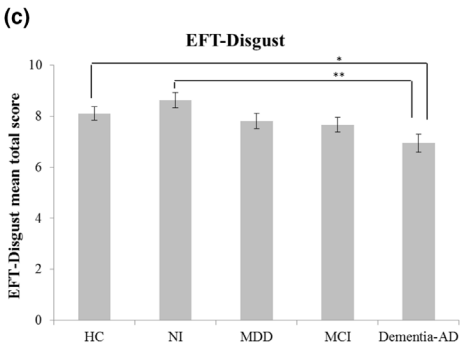
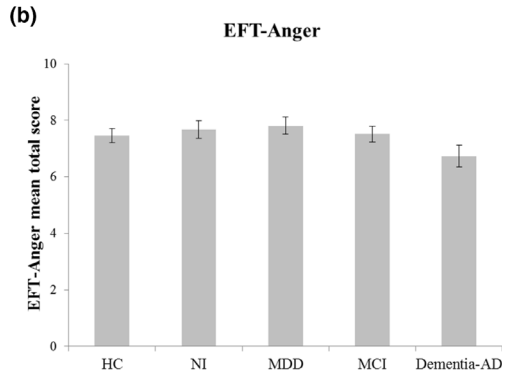
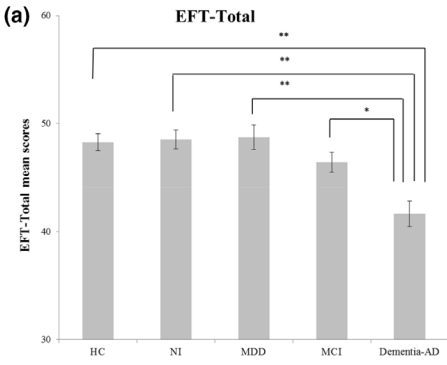


Table 3. General cognition (measured with MMSE) and memory performance (measured with RAVLT-IR and RAVLT-DR) in the HC, NI, MDD, MCI, and Dementia-AD groups. Displayed are means, standard errors, and test statistics (*F*, *df*) for ANCOVA with Age, Sex, and Education as covariates

	HC (<i>n</i> = 60) <i>M</i> (<i>SE</i>)	NI (<i>n</i> = 24) <i>M</i> (<i>SE</i>)	MDD (<i>n</i> = 27) <i>M</i> (<i>SE</i>)	MCI (<i>n</i> = 46) <i>M</i> (<i>SE</i>)	Dementia-AD (<i>n</i> = 42) <i>M</i> (<i>SE</i>)	<i>F</i> (<i>df</i>)	Sig.
MMSE	29.4 (0.1)	28.6 (0.2)	28.1 (0.3)	27.2 (0.4)	24.9 (0.4)	<i>F</i> (4,182) = 41.2	<i>p</i> < .01
RAVLT-IR	40.1 (1.3)	41.9 (1.8)	41.6 (1.8)	28.2 (1.0)	23.6 (1.1)	<i>F</i> (4,190) = 35.81	<i>p</i> < .01
RAVLT-DR	7.6 (0.4)	8.7 (0.5)	8.3 (0.5)	4.0 (0.4)	3.0 (0.4)	<i>F</i> (4,214) = 28.26	<i>p</i> < .01

Note. MMSE = Mini Mental State Examination. RAVLT-IR and RAVLT-DR = Rey Auditory Verbal Learning Test sum Immediate Recall trial 1–5 and Delayed Recall. Uncorrected Means (*M*) and Standard Errors (*SE*) are shown.

HC = Healthy Control, NI = No Impairment, MDD = Major Depressive Disorder, MCI = Mild Cognitive Impairment, Dementia-AD = Dementia of the Alzheimer's Disease Type.

$p < .01$) did have a significant individual contribution to our model, as well as EFT-Total (Model 2: $\chi^2 = 9.80, p = .04$). Adding EFT-Total to RAVLT-IR resulted in a final model that was highly significant ($\chi^2 = 132.23, p < .01$), with a large effect size (Nagelkerke Pseudo- $R^2 = .51$). In Table 4, the individual parameter estimates are shown per diagnostic category. Significant odds ratios < 1 (ORs) are found for RAVLT-IR in the MCI and Dementia-AD groups: with higher RAVLT-IR (predictor), the odds of a patient belonging to respectively MCI and Dementia-AD compared with HC significantly decrease. For EFT-Total, a significant OR < 1 is found in the Dementia-AD group: as EFT-total score is higher, the odds of patients belonging to the Dementia-AD group compared with HC decrease. No significant ORs were found for Age, or for the NI and MDD groups.

To assess whether the EFT-Total has significant value in differentiating between Dementia-AD and MCI, in addition to the RAVLT, a binomial logistic regression analysis was performed with group membership (only Dementia-AD and MCI) as dependent variable and RAVLT-IR and EFT-Total as predictor variables (see Table 5). First, RAVLT-IR had significant predictive power to discriminate between MCI and Dementia-AD (Model 1: $\chi^2 = 9.82, p < .01$). Second, in comparison to the model with only RAVLT-IR, adding EFT-Total was a significant improvement (Model 2: $\chi^2 = 9.95, p < .01$), resulting in a significant total model ($\chi^2 = 19.77, p < .01$), with a medium effect size (Nagelkerke

Table 4. Multinomial logistic regression analysis predicting group membership with Age, emotion recognition, as measured with EFT-Total, and memory performance, as measured with RAVLT-IR

	<i>B</i> (SE)	Wald	OR (95% CI)	<i>p</i> -value
NI				
Intercept	-1.84 (3.33)			
Age	0.00 (0.03)	<0.01	1.00 (0.95–1.06)	.95
RAVLT-IR	0.02 (0.03)	0.59	1.02 (0.97–1.08)	.44
EFT-Total	0.00 (0.04)	0.00	1.00 (0.92–1.09)	.99
MDD				
Intercept	1.74 (3.15)			
Age	-0.04 (0.03)	1.90	0.96 (0.91–1.02)	.17
RAVLT-IR	0.01 (0.03)	0.05	1.01 (0.96–1.06)	.82
EFT-Total	-0.01 (0.04)	0.03	0.99 (0.92–1.08)	.86
MCI				
Intercept	6.42 (2.94)			
Age	-0.03 (0.03)	1.16	0.97 (0.93–1.02)	.28
RAVLT-IR	-0.17 (0.03)	29.10	0.84 (0.79–0.90)	<.01
EFT-Total	0.02 (0.04)	0.22	1.02 (0.94–1.11)	.64
Dementia-AD				
Intercept	11.60 (3.33)			
Age	0.00 (0.03)	0.00	1.00 (0.94–1.06)	.98
RAVLT-IR	-0.24 (0.04)	35.04	0.78 (0.72–0.85)	<.01
EFT-Total	-0.10 (0.04)	5.31	0.91 (0.83–0.99)	.02

Note. the Healthy Control group was the reference category. *B*: Beta coefficient. SE: Standard Error. OR: Odds Ratio. 95% CI: 95% Confidence Interval.

NI = No Impairment, MDD = Major Depressive Disorder, MCI = Mild Cognitive Impairment, Dementia-AD = Dementia of the Alzheimer's Disease Type.

RAVLT-IR: Rey Auditory Verbal Learning Test sum Immediate Recall trial 1–5. EFT: EFT-Total = Ekman 60 Faces Test Total Score.

Table 5. Binomial logistic regression analysis predicting group membership (MCI or Dementia-AD) with emotion recognition, as measured with EFT-Total, and memory performance, as measured with RAVLT-IR

	B (SE)	Wald	OR (95% CI)	p-value
Model 1				
Constant	2.54 (0.93)			
RAVLT-IR	-0.10 (0.04)	8.33	0.90 (0.84–0.97)	<.01
Model 2				
Constant	7.28 (1.98)			
RAVLT-IR	-0.09 (0.04)	5.87	0.91 (0.85–0.98)	.02
EFT-Total	-0.11 (0.04)	8.37	0.89 (0.83–0.96)	<.01

Note. B: Beta coefficient. SE: Standard Error. OR: Odds Ratio. 95% CI: 95% Confidence Interval.

RAVLT-IR = Rey Auditory Verbal Learning Test sum Immediate Recall trial 1–5. EFT-Total = Ekman. 60 Faces Test Total Score.

Pseudo- $R^2 = .27$). In Table 5, a significant OR < 1 is found for RAVLT-IR in both Model 1 and Model 2: with higher RAVLT-IR scores, the odds of belonging to the Dementia-AD group compared with the MCI group significantly decrease. Furthermore, in Model 2 when in addition to RAVLT-IR, EFT-Total is higher, the odds of belonging to the Dementia-AD group compared with the MCI group significantly further decrease. In the final model, sensitivity was 66.7% and specificity was 69.9%.

In addition, the multinomial logistic regression analysis was repeated with RAVLT-IR and NER as predictor variables. NER in addition to RAVLT-IR did not significantly decrease unexplained variance; thus, it automatically was not added in the stepwise procedure.

Discussion

The aim of the present study was to investigate whether measurement of emotion recognition, an important aspect of social cognition, has added value for the classification of patients in a memory clinic, where patients mainly report memory complaints and concerns about Alzheimer's disease. It is not common clinical practice yet to assess social cognition as part of the standard neuropsychological examination in the memory clinic, even though social cognitive processes are assumed to underlie social behavioural changes, which in turn can be early markers of AD (Adolphs, 2009; David et al., 2016; Frith & Frith, 2012; Gallagher et al., 2011).

Our aim was to investigate whether testing emotion recognition in addition to episodic memory allowed for a more precise distinction between different diagnostic categories: amnesic MCI, Dementia-AD, or MDD. This was the first study to do so. We deem this very relevant, because the prognosis of MCI and MDD differs from that of Dementia-AD and requires different treatment approaches. We found that both patients diagnosed with Dementia-AD and MCI showed memory impairments, but only Dementia-AD patients had impaired emotion recognition, whereas MDD patients were unimpaired. Hence, combining measurement of episodic memory and emotion recognition allowed for a better distinction between diagnostic categories encountered in the memory clinic.

Patients with Dementia-AD had significantly worse performance on overall emotion recognition and specifically in recognizing disgust, fear, happiness, and sadness. Our findings added to several previous studies that emotion recognition adds significantly

explained variance to episodic memory as a discriminator between Dementia-AD and MCI. This was not investigated before. Regarding specific emotions, in addition to a statistically significant difference in recognizing happiness between Dementia-AD and MCI patients, we found Dementia-AD patients to have mainly worse recognition of negative emotions compared with control subjects, and then in particular fear, sadness, and disgust. Overall, our findings are in line with several previous reports, except for the recognition of disgust, which we found to be impaired in Dementia-AD patients (Henry et al., 2008; Phillips et al., 2010). Therefore, following up on Jorna et al. (2021) who reported on impaired NER in ABI patients, we additionally performed the logistic regression analysis with only negative emotions (NER) as a predictor variable. However, NER did not significantly differentiate between diagnostic categories, whereas overall emotion recognition performance, pertaining to aggregated score on the whole range of emotional expressions, did. Hence, for clinical use, this overall emotion recognition score has more merit than using a NER score only.

Given that episodic memory deficits are a core element of amnesic MCI and early AD, it is of course not surprising that we found both groups to perform significantly worse on the episodic memory test. However, we had not expected to find no differences between these two groups. This finding seems to contradict previous studies which reported verbal episodic memory tests to be good indicators of progression from MCI to Dementia-AD, suggesting an increase of the memory deficits (Belleville et al., 2017; Gainotti et al., 2014). Our MCI group was of the amnesic type, which deems it likely that for many patients, this was an early stage of AD. Apparently, conversion to dementia of the AD type is not mainly determined by an increase in memory impairment, but by impairment in other cognitive functions that interfere with daily life functioning, warranting a dementia diagnosis.

Our findings add clinical evidence to the view of Aggleton et al. (2016), who, based on an extensive literature review of human and animal studies, argue for a broader view on early neurodegeneration of the AD type, in which in addition to the medial temporal lobe and specifically the hippocampus, thalamic functioning and the Papez circuit are important. A further hypothesis they propose is that degeneration of thalamic structures may serve as a 'tipping point' for symptom expression. Our findings provide a neuropsychological argument for including impaired emotion recognition as marker for progression from MCI to dementia, in this 'tipping point' hypothesis. This makes sense because of the involvement of the thalamus and Papez circuit in memory processes (Vann & Nelson, 2015) as well as social cognition (Li et al., 2016).

In addition to deficits in emotion recognition and episodic memory, the Dementia-AD group had significant impaired general cognitive functioning, as measured with MMSE, in comparison with all other groups. Furthermore, MCI and MDD patients had worse general cognition compared with healthy controls, whereas they were not impaired in emotion recognition. This is not surprising, because we found episodic memory performance and MMSE to be highly correlated, and it was previously found that episodic memory is an important factor in the MMSE (Jones & Gallo, 2000). Thus, we assume there is great overlap between the concept of general cognition as measured with MMSE and episodic memory performance, which makes the similar correlations with emotion recognition obvious.

Overall, we found a significant relationship between general cognition and emotion recognition. However, when separating the different diagnostic categories, we did not find any specific relationships between general cognition and overall emotion recognition. Thus, our findings add to previous findings of an association between general cognition and emotion recognition performance, but not for deficits in general cognition

to explain impaired emotion recognition (Klein-Koerkamp et al., 2012; Phillips et al., 2010). Furthermore, as was previously reported, we found associations between the demographic characteristics age, level of education and sex, and overall emotion recognition, as well as with specific (negative) emotions (Calder et al., 2003; Kohler et al., 2011). However, after controlling for these demographic characteristics, significant differences in emotion recognition remained between diagnostic categories.

Our finding that MDD patients, who had reported memory complaints in our clinic, had no impairment on a performance-based memory test corroborates that other factors than memory impairment may underlie cognitive complaints in these patients. A previous study showed that MDD patients underestimated their cognitive functioning, as shown by a discrepancy between measures of subjective and objective cognitive performance (Schwert, Stohrer, Aschenbrenner, Weisbrod, & Schröder, 2018). The authors explained this by a negative bias in self-perception, as proposed by Beck (1987) in his cognitive model of depression. Following this model, it might be the case in our study that MDD patients present with cognitive complaints stemming from the depressive symptomatology itself, without there being any objective cognitive deficit caused by neurodegeneration.

In addition to intact episodic memory, MDD patients also had unimpaired emotion recognition, which we had not expected based on the literature (Dalili et al., 2015; Kohler et al., 2011). A difference from our study was that most previous studies included MDD patients in the whole adult age range, whereas we only investigated older patients. However, some included studies were performed with older MDD patients. In most of these studies, no significant differences were found between MDD patients and age-matched healthy control subjects in overall emotion recognition (Bertoux et al., 2012; Kan, Mimura, Kamijima, & Kawamura, 2004; Mah & Pollock, 2010). This is in line with our findings. However, these authors did find that MDD patients tended to overrate negative emotions, or interpret neutral or surprised faces and voices negatively. In two previous studies, specific emotion recognition deficits were found in older MDD patients: Sprengelmeyer et al. (2011) reported impaired recognition of disgust, but not in other emotions, and Phillips et al. (2010) reported mild impairments in the recognition of fear, sadness, and anger. This suggests a negative emotion recognition bias is present, which we did not find. However, we did not analyse whether in the errors made by MDD patients a negative bias was present, this would be interesting for future research.

It is important to note that patients were diagnosed based on formal diagnostic criteria. Even though social cognition is added as a core neurocognitive domain in the DSM-5, this domain is not yet part of the diagnostic criteria for AD, MCI, and MDD. Thus, a priori, the emotion recognition test was not used to classify patients as belonging to one of the diagnostic categories, as this was our main research question. In contrast, the episodic memory test was among other (visual) memory tests and tests measuring performance in other neurocognitive domains, as well as results of MRI scans, and in some cases biomarkers, part of the procedure in diagnosing Dementia-AD and MCI. Episodic memory decline is known to be an early marker of MCI and progression to Dementia-AD (Gainotti et al., 2014). Thus, we were not primarily interested in whether an episodic memory test discriminates between the aforementioned diagnostic groups, but to which extent an emotion recognition test showed added value in discriminating between groups visiting the memory clinic, including MCI and Dementia-AD.

Furthermore, in the current study we intentionally focussed on differentiating other diagnoses (i.e. MCI, MDD, and NI) from a single neurodegenerative disorder, being AD, whereas in clinical practice, other neurodegenerative disorders are also encountered in

the memory clinic, such as frontal temporal dementia (FTD) and vascular dementia. We are aware that this might limit the scope of our findings. Previous research did show the added value of measuring emotion recognition in differentiating between AD and FTD, with FTD patients performing significantly worse (Gossink et al., 2018). For future research, we would recommend to combine all the aforementioned diagnostic categories, as well as non-amnesic MCI, and assess whether emotion recognition distinguishes between all these groups, in comparison with other cognitive domains which are known to deteriorate in neurodegenerative diseases, such as executive- and visual spatial functioning (Fujie et al., 2008; Phillips et al., 2010). Moreover, our findings should be further investigated in a longitudinal study design in which pre-symptomatic, at-risk individuals are repeatedly tested on episodic memory and emotion recognition.

Conclusion

In conclusion, the addition of an emotion recognition test to an episodic memory test had significant value in differentiating patients with MCI from Dementia-AD, whereas both performed significantly worse than MDD patients. This is an important distinction since depression might be effectively treated if recognized as such. Therefore, we recommend adding a test of emotion recognition to the standard neuropsychological examination in the memory clinic: this contributes to establishing the causes and subsequent treatment options of neurocognitive complaints with which people present themselves in the memory clinic.

Conflicts of interest

All authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author upon reasonable request.

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Received 25 January 2021; revised version received 1 September 2021