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Envelhecimento e Défice Cognitivo:

Estudos de Adaptação, Validação e Normalização do

Montreal Cognitive Assessment (MoCA)

Faculdade de Psicologia e de Ciências da Educação

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“O valor das coisas não está no tempo que elas duram,

mas na intensidade com que acontecem.

Por isso existem momentos inesquecíveis,

coisas inexplicáveis e pessoas incomparáveis.”

(Fernando Pessoa)

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INTRODUÇÃO GERAL

Introdução Geral

O interesse em compreender a mente e o corpo foi transversal a tempos e civilizações, marcando decisivamente a história da Humanidade. A abordagem dualista da mente (outrora espírito ou alma) e do corpo (matéria ou cérebro) enquanto entidades distintas foi dominante até ao século XX. No entanto, a crescente percepção da necessidade de uma compreensão mais global, integrada e multidisciplinar da realidade humana, e da relação entre a funcionalidade do indivíduo e o sistema nervoso em particular, originou a eclosão das **Neurociências** cujo objectivo central era unificar o conhecimento dos processos neurobiológicos e psicobiológicos através da integração dos conhecimentos de diversas disciplinas como a Biologia, Neurologia, Psicologia, Química, Farmacologia, Genética ou a Informática (Kandel, 1996). A edificação desta ciência emergente ocorreu com o aparecimento das primeiras sociedades neurocientíficas, nomeadamente a pioneira norte-americana *Society for Neuroscience*, fundada em 1970 (Portellano, 2005).

O **desenvolvimento da Neuropsicologia enquanto uma disciplina científica diferenciada no âmbito das Neurociências** teve início em meados do século XX. Contudo, provavelmente o termo Neuropsicologia foi utilizado pela primeira vez por William Osler em 1913, tendo sido posteriormente popularizado em 1949 com a obra de Donald Hebb intilutada *The organization of behaviour: A neuropsychological theory* (Kristensen, Almeida & Gomes, 2001). Desde então, o conceito de **Neuropsicologia** foi definitivamente adoptado para designar a nova

disciplina de interface cujo objectivo central é o "estudo da relação entre o funcionamento neurológico e a actividade psicológica" (Simões, 1997, p. 138). Mais especificamente, a Neuropsicologia estuda as relações entre o sistema nervoso, comportamento e cognição tanto em indivíduos saudáveis como em pacientes que tenham sofrido algum tipo de dano cerebral, procurando ao mesmo tempo uma compreensão das bases neuronais dos processos cognitivos superiores (Portellano, 2005).

Em 1980, a ***American Psychological Association*** **(APA)** cria a **Divisão 40**: **Neuropsicologia Clínica**, vindo mais tarde, em 1996, a reconhecer a Neuropsicologia Clínica como uma especialidade, definindo-a como "uma especialidade que aplica os princípios da avaliação e intervenção, baseados no estudo científico do comportamento humano, ao funcionamento normal e anormal do sistema nervoso central (…) dedicada à compreensão das relações cérebro-comportamento e à aplicação de tais conhecimentos aos problemas humanos" (APA, 2011). A definição da ***American Academy of Clinical Neuropsychology*** é convergente ao apontar a Neuropsicologia Clínica como uma ciência aplicada que examina o impacto do normal e anormal funcionamento cerebral na ampla gama de funções cognitivas, emocionais e comportamentais (American Academy of Clinical Neuropsychology, 2007). Neste sentido, a prática da Neuropsicologia Clínica implica a integração de dados resultantes de vários métodos de avaliação, desde a entrevista clínica com o paciente, à história clínica e aos resultados obtidos em diversos instrumentos de avaliação, que permitam o exame da (dis)função cognitiva (APA, 2006).

No âmbito da prática clínica e da investigação em Neuropsicologia, a **avaliação neuropsicológica** assume um papel fundamental. Tendo como objectivo principal a determinação da integridade estrutural e funcional dos sistemas cerebrais (Simões, 1997), a avaliação neuropsicológica consiste "essencialmente num conjunto de procedimentos de exame clínico (…) e pode ser considerada como um aperfeiçoamento e alargamento da observação clínica que assenta na descrição mais precisa e fiável dos

desempenhos do paciente, através de instrumentos e procedimentos de teste especiais, que suscitam tipos de desempenho que não são acessíveis à observação clínica" (Benton, 1991, p.507).

A centralidade e relevância da avaliação neuropsicológica são bem exemplificadas na amplitude e diversidade dos seus **objectivos**, que podem incluir: 1) a caracterização das capacidades cognitivas e a determinação das modificações em relação ao nível pré-mórbido; 2) a predição das capacidades funcionais; 3) a análise dos sintomas e sinais presentes e identificação das patologias potencialmente subjacentes; 4) a recolha de informação útil ao estabelecimento do diagnóstico diferencial; 5) a recolha evidências para a análise da etiologia do quadro clínico; 6) o planeamento de procedimentos terapêuticos e preventivos adequados; 7) a monitorização da evolução da situação clínica; 8) a avaliação da eficácia de um procedimento terapêutico; 9) a identificação de populações de risco; 10) a avaliação do impacto cognitivo de patologias de foro extra neurológico; entre outros e para além dos fins de investigação, nomeadamente ao nível da operacionalização das hipóteses e objectivos dos estudos na área (Bartolomé & Ardila, 2005; Dastoor & Mohr, 1996; Guerreiro, 2005; Krishnan, 2007; Lezak, 2003; Morris & Kopelman, 1992; Sobral, 2006; Veríssimo, 2006).

Neste contexto, uma apropriada **selecção dos instrumentos de avaliação neuropsicológica** (número e conteúdo dos testes) constitui condição essencial para a validade e utilidade do processo de avaliação. Estes testes devem permitir uma **avaliação individualizada e compreensiva**, ajustando-se à natureza das queixas do paciente e do pedido de avaliação, aos dados relativos à situação clínica do indivíduo, às hipóteses diagnósticas suscitadas pelos desempenhos do indivíduo durante a avaliação, bem como às características contextuais de natureza social e cultural (American Academy of Clinical Neuropsychology, 2007; Simões, 1997).

Existem disponíveis diversos **tipos de instrumentos de avaliação neuropsicológica** que esquematicamente, e de modo algo artificial, podem ser categorizados em: 1) ***Instrumentos de Rasteio Cognitivo***, isto é, testes breves de administração fácil e rápida, que fornecem uma indicação aproximada das várias funções cognitivas e que são úteis quer na discriminação entre condição normal e patológica, quer na detecção primária de áreas lesadas; 2) ***Baterias de Avaliação Neuropsicológica Gerais****, fixas ou flexíveis*, constituídas por provas numerosas e diversificadas, cuja administração requer habitualmente algumas horas e que analisam mais detalhadamente as várias funções cognitivas; 3) ***Testes Específicos***, que podem ser utilizados isoladamente ou em combinações distintas e que permitem o exame mais individualizado e completo de determinada função cognitiva.

Neste plano, convém sublinhar os termos da distinção, sublinhados por Lonie, Tierney e Ebmeier (2009), entre testes de avaliação mais compreensiva, que correspondem a procedimentos de avaliação especializados e são mais utilizados nos cuidados de saúde secundários e terciários e os **testes de rastreio cognitivo breve**, que são de grande utilidade nos contextos em que é necessária uma breve triagem cognitiva, nomeadamente em contexto de cuidados de saúde primários e de rastreio na população comunitária.

Este constitui o enquadramento inicial do presente programa de investigação que procurou responder de modo prático ao problema da **identificação precoce do declínio cognitivo** num contexto de envelhecimento populacional e de aumento das taxas de prevalências das demências.

O aumento da esperança média de vida e o decréscimo das taxas de natalidade constituem alterações demográficas marcantes das últimas décadas nos países desenvolvidos. Estas mudanças traduzem uma

preocupante tendência para um **envelhecimento da população**. Uma exemplificação desta realidade inquietante encontra-se expressa nas estimativas do *Federal Interagency Forum on Aging-Related Statistics* (2000), que assinalam a evolução em 100 anos (1900-2000) da esperança média de vida nos EUA de 49 para 76.5 anos. No mesmo sentido, mas à escala mundial, Spar e La Rue (2002) mencionam que o número de pessoas com mais de 65 anos aumentou de cerca de 10 a 17 milhões, em 1900, para 342 milhões, em 1992, e espera-se que para aproximadamente 2.5 biliões (20% da população total) em 2050.

Em Portugal, a esperança média de vida aumentou de 66.7 anos para o sexo feminino e 61.1 anos para o sexo masculino, em 1960, para 82.2 e 75.9 anos, respectivamente, em 2007 (European Commission, 2010). De acordo com as estimativas de população residente de 2004 (Instituto Nacional de Estatística, 2004), a população idosa com 65 ou mais anos de idade representava já 17% do total da população portuguesa, tendo aumentado aproximadamente 3% na última década. O Índice de Envelhecimento (IE) da população portuguesa, traduzido pelo número de idosos por cada 100 jovens, era de 102, em 2000, tendo aumentado para 116, em 2009 (Instituto Nacional de Estatística, 2009). Projecções mais recentes indicam que Portugal irá manter a tendência de envelhecimento, estimando-se que o IE possa atingir os 398 idosos por cada 100 jovens, em 2050, o que representa mais do triplo do valor de 2009 (Instituto Nacional de Estatística, 2004). De acordo com esta tendência, estima-se que a população idosa represente mais de 32% do total da população portuguesa em 2060 (Instituto Nacional de Estatística, 2009).

De modo consensual, a idade tem sido considerada como o principal factor de risco para o desenvolvimento de demência, nomeadamente da **Doença de Alzheimer** (DA) (Chen, Lin, & Chen, 2009; Herrera-Rivero, Hernández-Aguilar, Manzo, & Aranda-Abreu, 2010; Seshadri et al., 1997) e, mais recentemente, do **Défice Cognitivo Ligeiro** (DCL) (Luck, Luppa, Briel, & Riedel-Heller, 2010). Numerosos estudos

epidemiológicos indicam um aumento da incidência da DA com a idade e um padrão aproximadamente exponencial das taxas de prevalência, que duplicam a cada cinco anos após os 60 anos. Deste modo, aos 60 anos a taxa de prevalência estimada é cerca de 0,7%, alcançando os 38,6% aos 90 anos (Barranco-Quintana, Allam, Castillo, & Navajas, 2005; Ferri et al., 2005; Jorm, Korten, & Henderson, 1987; McDowell, 2001; Santana, 2003).

Aproximadamente um século depois da primeira descrição clínica por Alzheimer, em que a DA era apresentada como uma doença rara, verifica-se um **crescimento abrupto do número de casos** desta forma de demência degenerativa, que se tornou numa das causas mais importantes de morbilidade nos idosos. De acordo com as estimativas mundiais, calcula-se que a DA afecte cerca de 24 a 25 milhões de pessoas, com cerca de 4,6 milhões de novos casos todos os anos (um novo caso a cada 7 segundos) (Ferri et al., 2005; Wimo, Winblad, Aguero-Torres, & von Strauss, 2004). Mais acresce que, num cenário de ausência de estratégias preventivas ou tratamentos eficazes, estima-se que o número de pacientes com demência duplicará a cada 20 anos, aproximando-se dos 42 milhões em 2020 e dos 81 milhões em 2040 (Ferri et al., 2005). As estimativas para Portugal, calculadas a partir dos estudos do Sul da Europa, sugerem que em 2010 existiam aproximadamente 153 mil pacientes com demência (Alzheimer Europe, 2010).

O envelhecimento demográfico e o drástico aumento das taxas de incidência e prevalência das demências com a idade explicam a sua enorme **relevância em termos assistenciais e de saúde pública a nível mundial** (Bassuk, Wypij, & Berkman, 2000; Comas-Herrera et al., 2011; Langa et al., 2001; Rice et al., 2001). Em 2006, a DA foi considerada a 5ª causa de morte mais frequente (Federal Interagency Forum on Aging-Related Statistics, 2010), posição que provavelmente seria superior caso tivessem sido contabilizadas todas as formas de demência. Contudo, talvez mais relevante do que a mortalidade atribuída à demência seja a **morbilidade** que lhe está associada. Neste sentido, estima-se que a

demência contribua com mais de 11,2% dos anos vividos com incapacidade nas pessoas acima dos 60 anos, valor superior ao calculado para os acidentes vasculares cerebrais (9,5%), para as doenças cardiovasculares (5,0%) ou para todas as formas de cancro (2,4%) (World Health Organization, 2003). Para além disto, diversos **custos** directos (associados ao tratamento, honorários profissionais, exames clínicos, hospitalizações, serviços de terceiros no apoio aos cuidados quotidianos do paciente, entre outros) e indirectos (abandono precoce da actividade profissional por parte do doente, diminuição da assiduidade laboral ou mesmo abandono da actividade profissional dos cuidadores informais, aumento da morbilidade nos prestadores de cuidados, entre outros) devem ser considerados no impacto que a demência tem sobre a economia da família, o sistema de saúde e o país em geral (Bassuk et al., 2000; Rice et al., 2001; Lurders & Storani, 2002). Contudo, ainda que a importância da detecção precoce do défice cognitivo, em especial na faixa de população mais vulnerável, ou seja, a população idosa, seja incontestável, ao nível dos **cuidados primários** esta tarefa é nos dias de hoje evidentemente deficitária, verificando-se uma **baixa sensibilidade à detecção das patologias no espectro da demência** (Kostopoulou, Delaney, & Munro, 2008; Löppönen, Räihä, Isoaho, Vahlberg, & Kivelä, 2003; Rait et al., 2010).

Em Portugal, a necessidade e o reconhecimento da "extraordinária importância" de uma **detecção precoce dos casos de DCL** encontra-se explicitamente contemplada no **Plano Nacional de Saúde 2004/2010**. Neste documento do Ministério da Saúde está formulada a previsão de 70 mil casos de DA, em Portugal, em 2010; existe uma chamada de atenção para a prioridade na detecção e seguimento de casos de DCL; as demências são sinalizadas como a principal causa de gastos na saúde acima dos 65 anos, esperando-se que estes gastos dupliquem nos próximos 10 anos; é reconhecida a sobrecarga que o doente com demência representa para as famílias, bem como a necessidade de dados epidemiológicos para uma estimação mais precisa desta problemática.

Neste contexto, torna-se **imperativo que o declínio cognitivo e a demência sejam detectados o mais precocemente possível e que o diagnóstico precoce se imponha como uma prioridade**. Na actualidade, a intervenção terapêutica já permite estabilizar ou melhorar os défices cognitivos, potencializar as capacidades funcionais e controlar os sintomas psicológicos associados, alongando assim o período de funcionamento relativamente preservado e potenciando a qualidade de vida dos pacientes e dos seus cuidadores, sendo que a eficácia terapêutica se encontra associada à precocidade da sua implementação (Cummings, 2003/2004; Kopman, 2003/2004; Sánchez & Sayago, 2000; Schimitt & Wichems, 2006). Num futuro próximo, as estratégias de intervenção preventivas ou curativas, poderão ainda ter um impacto mais relevante e directo no controlo da evolução ou regressão dos sintomas e, neste âmbito, a intervenção precoce será crucial.

Neste contexto, os **testes neuropsicológicos de rastreio cognitivo breve** continuam a ser o método de maior contributo para a **precocidade da detecção** das condições clínicas com défice cognitivo, incluindo os estados pré-demenciais, quer em estudos populacionais, quer ao nível dos cuidados de saúde primários (Cullen, O'Neill, Evans, Coen, & Lawlor, 2007; Fabrigoule, Barberger-Gateau, & Dartigues, 2006; Ismail & Shulman, 2006). Efectivamente, a capacidade para distinguir condições ao longo da continuidade entre o processo de envelhecimento normal e quadros clínicos é melhorada pela avaliação neuropsicológica (Smith & Ivnik, 2003/2004). Neste plano, Guerreiro (2005) lembra que a avaliação neuropsicológica constitui um dos exames complementares de diagnóstico de maior contributo para a precocidade na detecção de quadros demenciais.

Contudo, os resultados das avaliações neuropsicológicas podem ser fortemente comprometidos pela ausência de instrumentos reconhecidamente considerados de referência ou pela falta de cuidados

metodológicos no trabalho de adaptação cultural e linguística dos instrumentos utilizados e/ou pela inexistência de estudos de validação psicométrica e clínica dos seus resultados.

Deste modo, **a existência de instrumentos de avaliação neuropsicológica devidamente adaptados, validados e normalizados para a população portuguesa, que sejam sensíveis e precisos na discriminação entre o défice cognitivo patológico e o declínio cognitivo associado à idade, continua actualmente a ter especial importância**. Em Portugal, esta é uma necessidade ainda mais relevante dada a escassez de instrumentos representativos convenientemente adaptados e aferidos para a nossa população (Guerreiro, 2005; Simões, 1997).

O ***Mini-Mental State Examination*** (MMSE; Folstein, Folstein, & McHugh, 1975) constitui o instrumento de rastreio cognitivo breve mais utilizado em contexto clínico e de investigação, mais amplamente validado para diversas populações e mais referenciado na literatura. Com uma pontuação total de 30 pontos, esta prova é de administração fácil e rápida (5 a 10 minutos), permitindo uma avaliação global das funções cognitivas do indivíduo.

Em Portugal, o primeiro estudo sistemático com o MMSE foi realizado por Guerreiro (Guerreiro, Silva, Botelho, Leitão, Castro-Caldas & Garcia, 1994; Guerreiro, 1998). Para além do estudo de adaptação transcultural e da análise psicométrica, a autora elaborou dados de natureza normativa com base numa amostra de 137 controlos e realizou estudos de validação num grupo clínico heterogéneo de 151 pacientes. De acordo com a forte influência da escolaridade no desempenho na prova, os dados normativos e pontos de corte identificados foram definidos com base neste critério. Os pontos de corte mais adequados e que têm sido os mais utilizados nos estudos com a população portuguesa foram: I) Analfabetos: 15/16 pontos (sensibilidade = 63.6%; especificidade = 91.4%); II) 1 a 11

anos de escolaridade: 22/23 pontos (sensibilidade = 77.4%; especificidade = 96.8%); e III) mais de 11 anos de escolaridade: 27/28 pontos (sensibilidade = 66.7%; especificidade = 90%).

Mais recentemente, Morgado e colaboradores (2009) efectuaram uma actualização dos dados normativos do MMSE para a população portuguesa. O estudo foi conduzido numa amostra de 411 participantes da comunidade. Ainda que se tenha encontrado um efeito reduzido mas significativo da idade, este estudo corrobora que a escolaridade constitui a variável com maior capacidade preditiva do desempenho no teste. Deste modo, estes últimos dados normativos foram estabelecidos considerando três grupos de literacia: I) 0 a 2 anos (*M* = 25.16; *DP* = 2.16; ponto de corte: 22); II) 3 a 6 anos (*M* = 27.82; *DP* = 1.78; ponto de corte: 24); e III) 7 ou mais anos (*M* = 29.05; *DP* = 1.11; ponto de corte: 27).

Ambos os estudos normativos do MMSE para a população não contemplaram uma amostra estratificada e representativa da população portuguesa, sendo as respectivas amostras residentes apenas na área metropolitana de Lisboa. Por esta razão, está actualmente em curso, e numa fase avançada, a realização de um novo estudo normativo do MMSE na população portuguesa, com uma amostra estratificada por diversas variáveis sociodemográficas e representativa da população portuguesa.

Na década de 70, e do ponto de vista da avaliação cognitiva breve, esta prova constituiu um incontestável avanço, comparativamente aos testes de rastreio até então existentes, continuando actualmente a ser muito utilizada em estudos internacionais e nacionais e a representar uma linguagem comum na comunicação entre técnicos de saúde (nomeadamente, psicólogos, neurologistas e psiquiatras). Contudo, muitas são actualmente as **limitações apontadas ao MMSE** na literatura, designadamente: a baixa sensibilidade aos estádios de declínio cognitivo mais ligeiros, o que conduz a uma elevada taxa de falsos negativos e a uma relativa insensibilidade aos quadros clínicos de DCL; a reduzida complexidade de muitas das tarefas incluídas na prova, principalmente ao

nível da memória e da linguagem, o que gera um frequente efeito tecto dos desempenhos, sobretudos nos indivíduos com escolaridade mais elevada; a relativa incapacidade para diferenciar distintas condições clínicas; e, finalmente, a ausência de tarefas para a avaliação das funções executivas, o que compromete a sua sensibilidade na identificação de condições clínicas como a demência Frontotemporal (DFT) ou o défice cognitivo de origem vascular (Freitas, Santana & Simões, 2010; Ihl, Frölich, Martin, & Maurer, 1992; Naugle & Kawczak, 1989; Tombaugh & McIntyre, 1992; Wind et al., 1997).

Perante tais limitações, e numa tentativa de potenciar a eficácia e precisão do rastreio cognitivo, nomeadamente na identificação das formas mais ligeiras de declínio cognitivo, diversos **instrumentos de rastreio cognitivo alternativos** têm sido desenvolvidos nos últimos anos.

Neste contexto, o ***Montreal Cognitive Assessment*** (MoCA; Nasreddine et al., 2005), que é o objecto central do presente trabalho, constitui um dos testes de rastreio cognitivo breve mais recentes, e provavelmente o mais promissor entre estes, tendo sido desenvolvido especificamente para a avaliação das formas mais ligeiras de declínio cognitivo. O desenvolvimento desta prova estendeu-se ao longo de cinco anos, tendo sido efectuados sucessivos aperfeiçoamentos à sua estrutura (e.g., exclusão dos itens não discriminativos, redução do número de domínios cognitivos considerados, ajuste da pontuação dos itens de modo a valorizar diferenciadamente os itens mais discriminativos). A versão final deste instrumento constitui um método rápido, prático e eficaz no seu objectivo fundamental: a diferenciação entre alterações cognitivas devidas ao envelhecimento e défices cognitivos patológicos.

O MoCA é constituído por um protocolo de uma página, cujo tempo de aplicação é de aproximadamente 10 a 15 minutos, e inclui um manual onde são explicitadas as instruções para a administração dos itens e definido, de modo objectivo, o sistema de cotação do desempenho nos

itens. O teste permite obter uma pontuação máxima de 30 (pontos); as pontuações mais elevadas indicam melhores desempenhos. O MoCA avalia seis domínios cognitivos. As funções executivas são avaliadas através de uma tarefa adaptada do *Trail Making Test* B (1 ponto), de uma prova de fluência verbal fonémica (1 ponto) e de dois itens de semelhanças para a avaliação da capacidade de abstracção (2 pontos). A cópia do cubo (1 ponto) e o desenho do relógio (3 pontos) permitem o exame das capacidades visuoespaciais. A memória a curto prazo é avaliada através da aprendizagem de uma lista de 5 palavras em dois ensaios não pontuáveis com subsequente evocação diferida após 5 minutos (5 pontos). A atenção, concentração e memória de trabalho são examinadas através da repetição de uma sequência numérica em sentido directo (1 ponto) e em sentido inverso (1 ponto), de uma tarefa de cancelamento, e ainda de uma tarefa de subtracção em série (3 pontos). A nomeação de três animais pouco familiares (3 pontos), a repetição de duas frases sintacticamente complexas (2 pontos) e a prova de fluência verbal fonémica (1 ponto) contribuem para a mensuração das aptidões de linguagem. Por fim, quatro itens de orientação no tempo e dois itens de orientação no espaço compõem o domínio da orientação temporal e espacial. Neste conjunto de itens que constituem o MoCA estão incluídas 5 das 6 tarefas mais frequentemente usadas no rastreio da demência, de acordo com os resultados do estudo de Shulman e colaboradores (2006); o que potencia a rápida familiarização com o teste. A única medida não incluída no MoCA é o MMSE que surge, neste estudo, como a prova mais frequentemente utilizada neste contexto.

Comparativamente ao MMSE, o MoCA alarga o leque de funções cognitivas avaliadas, incluindo a avaliação das funções executivas, e apresenta itens mais exigentes e com maior nível de complexidade. Por exemplo, ao nível da avaliação da memória a curto prazo, o MoCA inclui mais palavras e maior intervalo de tempo precedente à evocação; as tarefas dirigidas às aptidões linguísticas são também mais complexas (ex. menor familiaridade na nomeação, maior complexidade sintáctica na repetição e

inclusão da prova de fluência fonémica), o mesmo ocorrendo ao nível do processamento visuoespacial (ex. cópia de desenho tridimensional e inclusão do desenho do relógio por instrução verbal), e da atenção, concentração e memória de trabalho (ex. inclusão da repetição das sequências numéricas e da prova de cancelamento). Deste modo, o MoCA proporciona **uma avaliação mais completa e mais exigente das funções cognitivas**, potenciando a sensibilidade dos seus resultados aos estádios de défice mais ligeiros e uma melhor adequação ao rastreio cognitivo dos indivíduos com escolaridade mais elevada.

Diversos estudos têm corroborado as **boas propriedades psicométricas** deste teste e a sua **elevada sensibilidade na identificação precoce de pacientes com DCL e DA** (Fujiwara et al., 2010; Lee et al., 2008; Koski, Xie, & Finch, 2009; Luis, Keegan, & Mullan, 2009; Nasreddine et al., 2005; Smith, Gildeh, & Holmes, 2007; Rahman & Gaafary, 2009; Zhao et al., 2011). No entanto, ainda que tenha sido originalmente desenvolvido para a avaliação cognitiva global destas populações clínicas, a sua precisão na identificação do declínio cognitivo mais ligeiro e os resultados consistente melhores do que o MMSE instigaram o uso cada vez mais generalizado do MoCA, e a **multiplicação dos estudos de validação a outras condições clínicas** [ex., Défice Cognitivo Vascular (Hachinski et al., 2006) e outras condições clínicas cerebrovasculares (Aggarwal & Kean, 2010; Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010); Doença de Parkinson (Hoops et al., 2009); Doença de Huntington (Videnovic et al., 2010); perturbações do sono (Gagnon, Postuma, Joncas, Desjardins & Latreille, 2010); população oncológica (Olson et al., 2010); HIV (Koski et al., 2011); perturbações de abuso de substâncias (Copersino et al., 2009); défice visual (Wittich, Phillips, Nasreddine, & Chertkow, 2010); entre outras].

O reconhecimento das vantagens do MoCA face ao MMSE, nomeadamente a superação das limitações apontadas a este último, a par da utilidade e eficácia corroboradas pelos estudos já realizados, impulsionaram a rápida **disseminação internacional** do MoCA que se

encontra actualmente adaptado e validado em 36 países. Para além disso, a importância do MoCA tem ainda sido regularmente realçada em vários **estudos comparativos** entre instrumentos de avaliação neuropsicológica (Lerch, Decker-Maruska, & Fleck, 2010; Zhao et al., 2011); **estudos de revisão** (Appels & Scherder, 2010; Ismail, Rajji, & Shulman, 2010; Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Levey, Lah, Goldstein, Steenland, & Bliwise, 2006; Lonie, Tierney, & Ebmeier, 2009; Moorhouse & Rockwood, 2008; Zhou & Zhao, 2009); e destacado em ***guidelines* relativas ao DCL e DA** (Chertkow et al., 2007; Gauthier et al., 2006, 2011; Robillard, 2007), mas também relativas a outras condições clínicas, nomeadamente ao Défice Cognitivo Vascular (Hachinski et al., 2006) e a **patologias cardiovasculares** (Arnold et al., 2007). Deste modo, e de acordo com a opinião expressa por alguns autores, o MoCA parece assumir um papel de relevo enquanto teste de rastreio cognitivo breve, estando *"em boa posição para se impor uma vez que recolhe a informação necessária através de um instrumento de rastreio eficaz e prático"* (Ismail & Shulman, 2006, p.525).

Deste modo, considerando as potencialidades apontadas ao MoCA e reconhecendo a importância da disponibilização de um instrumento com as suas características para a população portuguesa, e no seguimento de estudos prévios com uma primeira versão experimental, propusemo-nos a concretizar um plano de estudos que se pretendeu sistemático de modo a proporcionar as condições necessárias para o uso em Portugal deste instrumento de avaliação cognitiva, especificamente em contexto clínico e de investigação. Para tal, este projecto assumiu como objectivo geral orientador o desenvolvimento dos **estudos de adaptação, de validação psicométrica e clínica e de normalização do MoCA para a população portuguesa**. Os resultados da nossa investigação são apresentados sob a forma de **artigos científicos** que reflectem as diversas etapas percorridas para a consecução do objectivo geral definido. Cada um destes estudos atende a objectivos mais específicos delineados no âmbito de uma

investigação que no seu todo se complementam e articulam de modo coerente para permitir a disponibilização do MoCA aos clínicos e investigadores portugueses.

Desta forma, este trabalho encontra-se estruturado de acordo com os seguintes estudos:

O **Estudo I**, *Estudos de Adaptação do Montreal Cognitive Assessment (MoCA) para a população portuguesa* (Freitas, Simões, Martins, Vilar & Santana, 2010), centra-se na descrição do processo de adaptação transcultural do MoCA para a população portuguesa e na análise da equivalência entre a versão original e a versão final portuguesa. O processo de adaptação transcultural constituiu a primeira etapa deste plano de estudos, tendo seguido as orientações metodológicas habituais neste tipo de estudos a fim de assegurar o rigor deste procedimento, comparável ao desenvolvimento de um novo instrumento. A procura do máximo de equivalência entre o instrumento original e a versão portuguesa e a preocupação com a validade ecológica do instrumento na população portuguesa conduziram este longo processo, do qual resultou a versão final portuguesa do MoCA e do respectivo manual de administração e cotação.

O **Estudo II**, *Montreal Cognitive Assessment (MoCA): Influence of sociodemographic and health variables* (Freitas, Simões, Alves & Santana, 2012), analisa a influência das variáveis sociodemográficas (idade, escolaridade, género, estado civil, situação profissional, região geográfica, localização geográfica (litoral/interior) e área de residência) e de saúde (história familiar de demência, sintomatologia depressiva e queixas subjectivas de memória) nos resultados no MoCA, numa amostra da comunidade, estratificada de acordo com as variáveis sociodemográficas consideradas relevantes e representativa da população portuguesa. O facto de diversos estudos demonstrarem a influência de determinadas variáveis sociodemográficas e de saúde no desempenho em testes de rastreio

cognitivo, a inexistência de estudos que, com recurso a uma amostra estratificada da população portuguesa, tenham analisado a influência das variáveis sociodemográficas no desempenho em testes de rastreio cognitivo, a surpreendente ausência de estudos internacionais similares com o MoCA e a controvérsia inerente aos estudos que analisam a influência das variáveis de saúde em testes de rastreio cognitivo, impulsionaram fortemente a realização deste estudo. Este estudo constitui um contributo importante para a compreensão das possíveis fontes de enviesamento que podem advir das características individuais, permitindo, em última análise uma interpretação mais idiossincrática dos resultados da avaliação.

O **Estudo III**, *Construct validity of the Montreal Cognitive Assessment (MoCA)* (Freitas, Simões, Marôco, Alves & Santana, 2012), incide sobre a estrutura factorial do MoCA. Pretendeu-se examinar as propriedades psicométricas dos itens do teste e analisar a sua estrutura interna, testando diversos modelos através da análise factorial confirmatória, com recurso a uma amostra de indivíduos cognitivamente saudáveis e de pacientes com DCL e DA, e avaliando a respectiva validade factorial, convergente e discriminante (estudo de validade de constructo). Apesar do actual uso generalizado do MoCA a nível internacional e dos diversos estudos de validação publicados, a estrutura interna do instrumento continua a necessitar de estudos mais sistemáticos. Este estudo contribui para ultrapassar esta significativa lacuna na avaliação da validade de constructo deste instrumento e reúne novas evidências da validade do MoCA favoráveis à utilização de perfis de desempenho tendo em conta os diferentes domínios cognitivos latentes, permitindo assim um exame mais informativo do perfil cognitivo individual.

O **Estudo IV**, *Montreal Cognitive Assessment (MoCA): Validation study for Mild Cognitive Impairment and Alzheimer´s Disease* (Freitas,

Simões, Alves & Santana, 2012), é o primeiro de três estudos específicos de validação clínica e tem por objectivo a validação do MoCA em pacientes com DCL e DA. São analisadas as propriedades psicométricas do teste, indicada a sua precisão diagnóstica e valores preditivos, e são definidos os pontos de corte óptimos para cada um dos grupos clínicos considerados. São ainda analisados dados de natureza longitudinal com o objectivo de investigar a sensibilidade do MoCA ao declínio progressivo num curto espaço de tempo. Com este estudo pretendemos avaliar a capacidade do MoCA para detectar precocemente o declínio cognitivo, a sua capacidade de diferenciação fundamental entre as alterações cognitivas patológicas e as modificações cognitivas inerentes ao envelhecimento, bem como a sensibilidade dos seus resultados à progressão do declínio cognitivo, corroborando sucessivamente a sua utilidade enquanto teste de rastreio cognitivo e de monitorização da condição clínica dos pacientes portugueses com DCL e DA.

O **Estudo V**, *Validity study of the Montreal Cognitive Assessment (MoCA) in patients with Frontotemporal Dementia* (Freitas, Simões, Alves, Duro & Santana, *submitted*) visa a validação do MoCA para o rastreio cognitivo de pacientes com variante comportamental da DFT, sendo examinadas as propriedades psicométricas da prova, estabelecido o ponto de corte óptimo para este grupo clínico, e avaliada a precisão diagnóstica e valor preditivo dos seus resultados. Adicionalmente, é ainda investigado o perfil cognitivo destes pacientes no MoCA e são analisadas as diferenças comparativamente aos pacientes com DA. As elevadas taxas de prevalência da DFT, a baixa sensibilidade do MMSE à detecção do défice cognitivo nestes pacientes amplamente reportada nos estudos publicados, a ausência de estudos de validação do MoCA enquanto teste de rastreio cognitivo nos pacientes com variante comportamental da DFT e a necessidade de um teste sensível, fiável e preciso para a avaliação breve do défice cognitivo

nestes pacientes constituíram incentivos importantes para a realização deste estudo.

O **Estudo VI**, *Montreal Cognitive Assessment (MoCA): Validation study for Vascular Dementia* (Freitas, Simões, Alves, Vicente & Santana, *submitted*) tem por objectivo a validação do MoCA em pacientes com demência Vascular (DV). As elevadas taxas de prevalência apontadas pelos estudos epidemiológicos que indicam que a DV constitui a segunda causa mais frequente de demência, a natureza provavelmente tratável do défice cognitivo vascular adquirido, a relevância da implementação de estratégias preventivas nestes pacientes, e os avanços recentes ao nível dos tratamentos farmacológicos destacam uma vez mais a importância da existência de um instrumento breve de avaliação cognitiva eficaz na detecção dos estádios precoces da DV. Neste contexto, os recentes *NINDS-CSN VCI Harmonization Standards criteria* (Hachinski et al., 2006) recomendam o uso de uma versão abreviada do MoCA para o rastreio cognitivo em pacientes vasculares. Contudo, ainda que existam estudos de validação do MoCA em pacientes do foro vascular, um estudo que contemple pacientes com DV 'pura' e que investigue a eficácia da versão abreviada proposta pelos *NINDS-CSN VCI Harmonization Standards criteria* assume carácter pioneiro. Por isso, neste estudo pretendeu-se analisar as propriedades psicométricas do MoCA neste grupo clínico, estabelecer o ponto de corte óptimo para a identificação destes pacientes e identificar a respectiva precisão diagnóstica e valor preditivo, sendo que tais análises são duplamente realizadas, considerando o MoCA escala completa e a versão abreviada proposta pelos *NINDS-CSN VCI Harmonization Standards criteria*. Adicionalmente, neste estudo é ainda examinado o perfil cognitivo destes pacientes no MoCA e são analisadas as diferenças comparativamente aos pacientes com DA.

O **Estudo VII**, *Montreal Cognitive Assessment (MoCA): Normative study for the Portuguese population* (Freitas, Simões, Alves & Santana, 2011), teve como objectivo principal o estabelecimento de dados normativos para a população portuguesa, com base numa amostra da comunidade, estratificada e representativa da população portuguesa, constituída por adultos cognitivamente saudáveis. Apesar dos estudos prévios corroborarem as excelentes propriedades psicométricas do MoCA, bem como a sua precisão diagnóstica em diferentes contextos clínicos, a utilidade clínica da prova ficaria muito limitada caso não fossem igualmente disponibilizados dados de natureza normativa. O acesso a normas representativas viabilizará a comparação de pacientes com outras patologias, para além daquelas que foram alvo de validação clínica, com os respectivos grupos de referência cognitivamente saudáveis (Estudos IV, V e VI).

Por fim, é apresentada uma **Discussão Geral** dos resultados deste plano de trabalhos, onde são sintetizados e escrutinados os **principais resultados** da presente investigação, analisadas as principais **limitações**, bem como articuladas as principais **conclusões e implicações para a prática clínica e de investigação em Portugal**.

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ESTUDO I

Estudos de Adaptação do Montreal Cognitive Assessment (MoCA) para a população portuguesa

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Resumo

O *Montreal Cognitive Assessment* (MoCA) é um instrumento de rastreio cognitivo mais sensível que o *Mini-Mental State Examination* (MMSE) aos estádios mais ligeiros de declínio, nomeadamente ao Défice Cognitivo Ligeiro (DCL), que frequentemente progride para Demência. Este trabalho descreve as etapas do processo de adaptação transcultural do MoCA para a população portuguesa e analisa a equivalência entre a versão original e a versão final portuguesa. O processo envolveu a tradução, retroversão, aperfeiçoamento linguístico do instrumento e manual, estudos com a versão experimental, revisão e ajustamentos necessários para finalizar a versão portuguesa, e análise da equivalência com a versão original. Os estudos realizados evidenciam as boas propriedades psicométricas dos resultados com a versão portuguesa do MoCA, a sua validade, utilidade clínica e equivalência com a prova original, nos diversos níveis considerados. O MoCA é um instrumento privilegiado na detecção precoce do declínio cognitivo e está convenientemente adaptado para a população portuguesa.

Palavras-Chave: Montreal Cognitive Assessment (MoCA); Rastreio Cognitivo; Défice Cognitivo Ligeiro; Doença de Alzheimer.

INTRODUÇÃO

O Défice Cognitivo Ligeiro (DCL) é uma entidade clínica intermédia entre as alterações cognitivas do envelhecimento e as primeiras manifestações clínicas da demência. Esta concepção reúne o consenso da maioria dos investigadores e encontra sustentação empírica em numerosos estudos (e.g., Gauthier et al., 2006; Petersen & O´Brien, 2006; Cargin et al., 2005; Winblad et al., 2004; Petersen, 2003/2004, 2007).

Originalmente, os critérios diagnósticos para o DCL focavam os défices de memória e a esta condição estava associado um elevado risco de progressão para a Doença de Alzheimer (DA) (Petersen et al., 1999). Contudo, o drástico aumento da investigação no âmbito do DCL (Petersen & O´Brien, 2006) conduziu à crescente evidência de que alguns pacientes progrediam para outros tipos de demência, surgindo a necessidade de tornar o conceito de DCL mais abrangente, de forma a incluir outros perfis de défice cognitivo que tendiam a preceder outros tipos de demência (e.g., Winblad et al., 2004; Petersen, 2004, 2007; Gauthier et al., 2006).

Assim, de acordo com os actuais critérios internacionais, adoptados pelo *National Institute on Aging Alzheimer´s Disease Centers Program* e pela *Alzheimer´s Disease Neuroimaging Initiative*, o diagnóstico de DCL implica a existência de queixas cognitivas e de um défice objectivo, ou seja, um desempenho em testes de avaliação inferior ao esperado para a idade e/ou escolaridade; este défice não é suficientemente severo para o estabelecimento do diagnóstico de uma demência, nem para interferir de modo significativo na capacidade funcional do indivíduo que mantém as suas actividades de vida diária praticamente normais (Petersen, 2004; Petersen & O´Brien, 2006). Mais acresce a consensualidade na subdivisão do DCL em DCL-amnésico e DCL-não-amnésico (de acordo com a presença ou não de défice de memória), sendo que cada um destes subtipos se subdivide ainda em domínio único ou múltiplos domínios (de acordo com a presença de um ou mais domínios cognitivos afectados), perfazendo assim a existência de quatro subtipos de DCL: DCL-amnésico

domínio único, DCL-amnésico múltiplos domínios, DCL-não-amnésico domínio único e DCL-não-amnésico múltiplos domínios. Nestes moldes e com base numa vasta matriz de evidências clínicas, o DCL tem sido proposto como entidade diagnóstica para o DSM-V (Petersen & O´Brien, 2006).

Com uma taxa de conversão anual para a demência de cerca de 12% (Petersen et al., 1999), muito superior à encontrada na população normal, de cerca de 1 a 2% (Petersen, 2000), e com estudos longitudinais que revelam que cerca de 80% dos indivíduos com DCL progrediram para demência ao fim de 6 anos (Petersen & Morris, 2003/2004), o DCL tem-se consagrado como uma entidade clínica de elevado risco para a demência. Deste modo, actualmente, o DCL assume um papel central na identificação precoce da demência (Mueller et al., 2005) e tende a assumir o papel preferencial, comparativamente com a DA, de objecto de estudo dos investigadores no espectro do Alzheimer, *"um facto que resulta da relativa falência das estratégias de tratamento na fase já sintomática de demência"* (Santana, 2003, p.99).

Caracterização do Montreal Cognitive Assessment (MoCA)

O *Montreal Cognitive Assessment* (MoCA; Nasreddine et al., 2005) constitui um instrumento breve de rastreio cognitivo. Originalmente desenhado para o rastreio do DCL, o processo de construção do teste prolongou-se ao longo de cinco anos, tendo sido efectuados sucessivos aperfeiçoamentos à sua estrutura (e.g., exclusão de 5 itens que não se revelaram discriminativos, redução do número de domínios cognitivos, ajuste da pontuação dos itens de modo a valorizar mais os itens mais discriminativos – Nasreddine et al., 2005).

A versão final deste instrumento representa um método rápido, prático e eficaz na distinção entre desempenhos de adultos com envelhecimento cognitivo normal e adultos com défice cognitivo, para além

de se mostrar útil na avaliação de estádios intermédios de défice cognitivo, nomeadamente do DCL e da DA ligeira e moderada. Deste modo, o MoCA apresenta potencial utilidade na elaboração de directrizes para futuras investigações acerca do DCL (Nasreddine et al., 2005).

O MoCA é constituído por um protocolo de uma página, cujo tempo de aplicação é de aproximadamente 10 minutos, e por um manual onde são explicitadas as instruções para a administração das provas e definido, de modo objectivo, o sistema de cotação do desempenho nos itens. Com uma pontuação máxima de 30 (pontos), o MoCA avalia seis domínios cognitivos contemplando diversas tarefas em cada domínio, de acordo com a estrutura descrita na Tabela 1 (Nasreddine et al., 2005). No conjunto de itens que constituem este instrumento estão incluídas 5 das 6 tarefas mais frequentemente usadas no rastreio da demência, de acordo com o resultado da pesquisa do IPA (Shulman et al., 2006).

Comparativamente ao conhecido *Mini-Mental State Examination* (MMSE; Folstein, Folstein & McHugh, 1975; Guerreiro, 1998), o MoCA avalia mais funções cognitivas e apresenta itens com maior nível de complexidade. Efectivamente, a tarefa de memória do MoCA implica mais palavras e maior intervalo de tempo precedente à evocação. No mesmo sentido, deve ser referida a presença de tarefas de avaliação das funções executivas, a maior exigência ao nível das aptidões linguísticas, do processamento visuoespacial complexo, e da atenção, concentração e memória de trabalho (áreas de potencial deterioração nos pacientes com DCL). Deste modo, O MoCA configura-se como um instrumento mais sensível aos estádios de défice mais ligeiros e mais adequado ao rastreio cognitivo da população com escolaridade mais elevada. (Freitas, Simões & Santana, 2008a; Freitas, Simões & Santana, 2008b; Freitas, Pinto, Duro, Santiago, Simões & Santana, 2009; Lee et al., 2008; Luis, Keegan & Mullan, 2009; Nasreddine et al., 2005; Trenkle, Shankle & Azen, 2007).

Tabela 1. Estrutura do MoCA

Domínio Cognitivo	Tarefas	Pontuação
Função Executiva	*Trail Making Test* B (adaptado)	1 ponto
	Fluência Verbal Fonémica	1 ponto
	Abstracção Verbal	2 pontos
Capacidade Visuo-espacial	Desenho do Relógio	3 pontos
	Cópia do Cubo	1 ponto
Memória	Evocação Diferida de Palavras (5 minutos)	5 pontos
Atenção, Concentração e Memória de Trabalho	Memória de dígitos (sentido directo)	1 ponto
	Memória de dígitos (sentido inverso)	1 ponto
	Tarefa de Cancelamento	1 ponto
	Subtracção em série de 7	3 pontos
Linguagem	Nomeação de 3 animais pouco familiares	3 pontos
	Repetição de 2 frases complexas	2 pontos
	Fluência Verbal Fonémica (supracitada)	1 ponto
Orientação	Temporal	4 pontos
	Espacial	2 pontos

Levey, Lah, Goldstein, Steenland e Bliwise (2006) acrescentam que o MoCA pode auxiliar na diferenciação entre subtipos de DCL, na medida em que inclui itens como a aprendizagem da lista de palavras e respectiva evocação diferida, que seriam mais sensíveis ao DCL tipo amnésico, mas também avalia outros domínios cognitivos (e.g. função executiva, linguagem, capacidade visuoespacial) que podem contribuir para a avaliação de outros subtipos de DCL.

O teste pode, ainda, fornecer uma estimativa quantitativa da capacidade cognitiva, e não apenas qualitativa (no sentido de identificar um desempenho normal ou a presença de défice), ampliando e potenciando deste modo a sua utilidade para monitorizar a magnitude das alterações das

capacidades cognitivas associadas à evolução da patologia ou resultantes de estratégias de intervenção (Koski, Xie & Finch, 2009).

O MoCA tem sido considerado como um teste de rastreio cognitivo privilegiado (Gauthier et al., 2006), uma vez que *"constitui um método eficaz para rastrear o Défice Cognitivo Ligeiro e distingui-lo* [do perfil cognitivo] *de idosos com função cognitiva intacta"*, estando *"em boa posição para se impor, uma vez que recolhe a informação necessária através de um instrumento de rastreio eficaz e prático"* (Ismail & Shulman, 2006, p.525). Neste sentido, o MoCA é referido, nas recomendações do *Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia*, como o instrumento a usar em caso de suspeita de DCL (Jacova, Kertesz, Blair, Fisk & Feldman, 2007). Na revisão de Lonie, Tierney e Ebmeier (2009), o MoCA surge como um dos quatro instrumentos mais sensíveis na detecção do DCL e da DA Ligeira. Relevância semelhante é concluída na revisão de Ismail, Rajji e Shulman (2009) que consideram que o MoCA tem ganho credibilidade, devido à sua elevada sensibilidade ao DCL, ao facto de avaliar o funcionamento executivo e ao reduzido enviesamento cultural dos seus itens.

O presente trabalho tem por objectivo central descrever as etapas do processo de adaptação transcultural do MoCA para a população portuguesa. Pretende-se ainda analisar a equivalência entre a versão original e a Versão Final Portuguesa.

Estudos Internacionais

Os estudos originalmente realizados (Nasreddine et al., 2005) indicam que o MoCA possui boa consistência interna (α Cronbach = .83), elevada fiabilidade teste-reteste (r = .92, p < .001, ± 26 dias), equivalência linguística (nas versões em inglês e em francês), e utilidade em contexto hospitalar, comunitário e de investigação. Relativamente à validade

concorrente, os seus resultados apresentam uma correlação elevada com os obtidos no MMSE (r = .87, p < .001). Neste estudo, o MoCA revelou-se, ainda, eficaz na distinção entre os grupos Controlo, DCL e DA ($F_{(2,274)}$ = 232.91, EPM = 12.84, p < .001), diferença que se manteve significativa mesmo depois de controlados os efeitos das variáveis idade e escolaridade (Covariância: $F_{(2,269)}$ = 183.32, EPM = 11.18, p < .001). Esta capacidade de diferenciação é, aliás, superior à observada com o MMSE. Assim, com um ponto de corte óptimo de 26 pontos, o MoCA possui uma excelente sensibilidade na identificação do DCL e da DA (90% e 100%, respectivamente), comparativamente aos resultados modestos do MMSE (18% e 78%). No que respeita à especificidade, o MoCA possui uma "boa a muito boa" especificidade, tendo identificado correctamente 87% dos participantes cognitivamente saudáveis, tendo o MMSE apresentado resultados de 100%.

Os estudos de adaptação e validação do MoCA decorrem, actualmente, em 30 países (www.mocatest.org), o que reflecte bem a utilidade e importância reconhecida a este instrumento. Os diversos estudos internacionais comprovam as boas propriedades psicométricas da prova [e.g.: α Cronbach de .90 e correlação com resultados no MMSE de .83, p < .001 (Fontini et al., 2007); α Cronbach de .83 e estabilidade temporal teste-reteste de .92, p < .001, 35.0 (± 17.6) dias (Rahman & Gaafary (2009)] e a sua sensibilidade ao declínio cognitivo, corroborando a sua eficácia enquanto teste de rastreio cognitivo, não só para o DCL e DA (cf. Tabela 2) mas, também, para o declínio cognitivo associado a outros quadros clínicos, verificando-se uma crescente generalização da utilização clínica da prova [e.g.: Doença de Parkinson (Gill, Freshman, Blender & Ravina, 2008; Nazem et al., 2009; Wilner, 2008; Zadikoff et al., 2008); Doença de Huntington (Corey-Bloom, Goldstein, Lessig, Peavy & Jacobson, 2009); Doença Cerebrovascular (Martinic-Popović, Šerić & Demarin, 2006; Martinic-Popović, Šerić & Demarin, 2007); Metástases Cerebrais (Olson, Chhanabhai & McKenzie, 2008)].

Tabela 2. Estudos de validação clínica

Estudo	População	MoCA		MMSE	
		Sensib.	Espec.	Sensib.	Espec.
Smith et al., 2007	DCL	83%	50%	17%	100%
	Demência	94%		25%	
Lee et al., 2008	DCL	89%	84%	--	--
	DA	98%			
Wen et al. , 2008	DCL	92%	--	24%	--
Luis et al., 2009	DCL	96%	95%	58%	84%
Rahman & Gaafary, 2009	DCL	92%	86%	--	--

Abreviaturas: Sensib. = Sensibilidade; Espec. = Especificidade; DCL = Défice Cognitivo Ligeiro; DA = Doença de Alzheimer.

MÉTODO

O processo de adaptação transcultural do MoCA para a população portuguesa passou por diversas etapas, até à obtenção da Versão Final Portuguesa (Simões, Freitas, Santana, Firmino, Martins, Nasreddine & Vilar, 2008). A figura 1 ilustra as etapas deste processo.

Fase 1: Autorização

A autorização para a realização de estudos de adaptação, validação e aferição do MoCA para a população portuguesa foi solicitada e concedida em 2006, pelos autores da prova original. A tradução para português da prova e do respectivo manual de instruções de administração e cotação (Versão Experimental) foi realizada nesse mesmo ano.

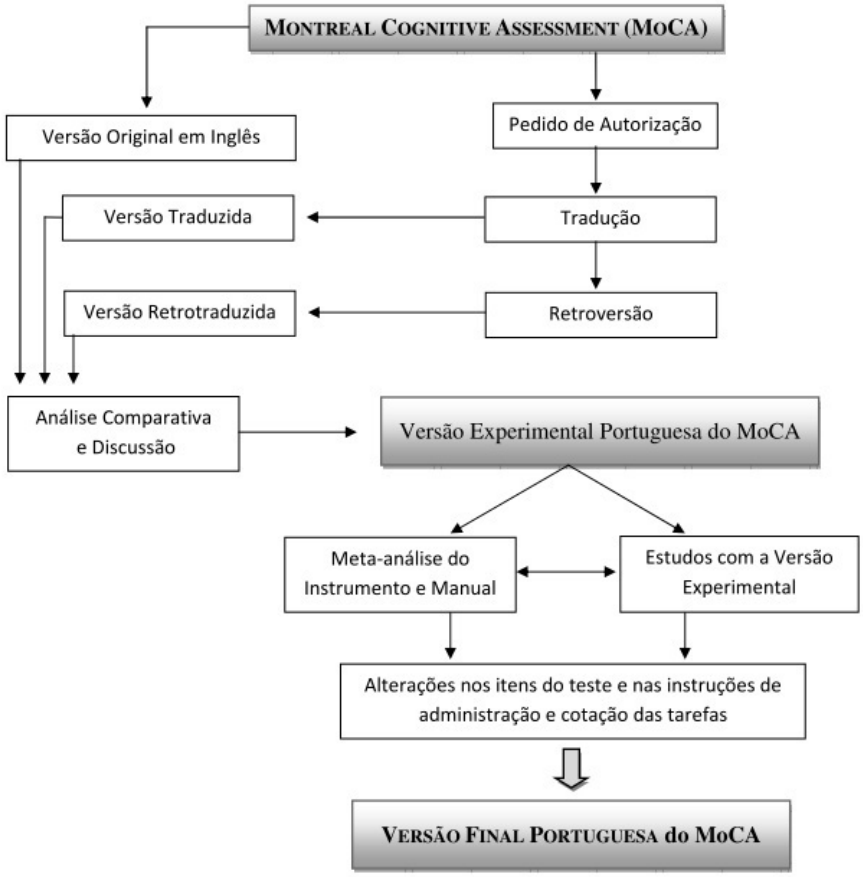

Figura 1. Etapas do processo de adaptação do MoCA para a população portuguesa.

Fase 2: Tradução e Retroversão

Inicialmente, duas traduções, do original em inglês para o português, foram realizadas independentemente por psicólogos fluentes na língua inglesa e com experiência nas tarefas de adaptação de testes de avaliação cognitiva. De seguida, a equipa responsável pelos estudos do MoCA em Portugal avaliou e discutiu tais traduções, chegando a uma

versão única. Posteriormente, um tradutor bilingue, sem conhecimento da versão original da prova, efectuou a retroversão para inglês da versão portuguesa. A tradução e retroversão foram discutidas e comparadas com o original para identificar discrepâncias entre a fonte e o alvo e se incrementar a equivalência entre as versões. Procurou-se obter equivalência semântica (equivalência entre as palavras quanto ao sentido que veiculam e à abrangência do mesmo), idiomática (equivalência de expressões típicas, cujo significado não pode ser depreendido literalmente) e experimental (adequação de palavras ao contexto cultural alvo), tendo-se, através deste processo, chegado à Versão Experimental Portuguesa do MoCA (Simões, Firmino, Vilar & Martins, 2007).

Fase 3: Estudos com a Versão Experimental Portuguesa

A Versão Experimental Portuguesa do MoCA foi alvo de diversos estudos que procuraram averiguar a aplicabilidade da prova na população portuguesa, respectivas qualidades psicométricas e capacidade diagnóstica. Estes estudos tiveram ainda por objectivo salientar aspectos passíveis de aperfeiçoamento.

Num primeiro trabalho, Martins (2007) analisou o desempenho de 325 adultos idosos, divididos em três grupos: I) 153 adultos saudáveis (critérios de inclusão: função cognitiva global normal, independência funcional e comportamento social adequado), II) 72 pacientes com Défice Cognitivo Ligeiro (critérios diagnósticos: Petersen et al., 1999) e III) 100 pacientes com Demência (critérios diagnósticos: queixas mnésicas, confirmadas pelo cuidador e por testes de avaliação neuropsicológica; défices cognitivos que incluem afasia, apraxia, agnosia e/ou perturbação na capacidade de execução; e impacto significativo dos défices na vida social e ocupacional do idoso). A autora concluiu que o MoCA (Versão Experimental Portuguesa) apresenta boas características psicométricas e é adequado ao rastreio do défice cognitivo na nossa população. Os resultados revelaram uma excelente consistência interna (α Cronbach = .94), excelente

estabilidade temporal dos resultados teste-reteste [r = .85, p < .001; intervalo médio de 33.5 dias)], e correlações variando entre modestas (r = .59) a perfeitas (r = 1.00) para o acordo inter-avaliadores, consoante os itens em questão. Na análise dos itens, foram encontrados os seguintes resultados: correlações inter-item significativamente positivas entre todos os itens sendo, de acordo com o esperado, superiores entre os itens constituintes de um mesmo domínio cognitivo; correlações item-total sempre superiores a .20, sugerindo assim que todos os itens do teste apresentam poder discriminativo; e um índice de dificuldade dos itens adequado para sujeitos com DCL (média do índice de dificuldade dos itens = .56). O MoCA revelou-se eficaz na diferenciação dos três grupos entre si ($F_{(2,324)}$ = 295.037, p < .001); tendo o grupo controlo uma média de pontuações mais elevada (22.46 ± 5.08) do que os grupos clínicos, seguindo-se o grupo com DCL (15.86 ± 4.03) e, por fim, o grupo com Demência (8.69 ± 3.53).

Freitas e colaboradores (2008a; 2008b) analisaram as características psicométricas da Versão Experimental do MoCA num grupo de idosos saudáveis (n = 80), residentes na comunidade [Idade ≥ 50 anos (62.91 ± 9.39; *Min* = 50, *Máx* = 84)]. Os critérios para a inclusão no grupo de idosos saudáveis foram: a) consentimento informado; b) português como língua materna e escolaridade realizada em Portugal; c) idade ≥ a 50 anos; c) pontuação normal no MMSE, de acordo com os dados normativos para a população portuguesa (Guerreiro, 1998); d) independência e funcionalidade preservadas; e) ausência de sintomatologia depressiva grave (pontuação na *Geriatric Depression Scale* (GDS) < 20); f) ausência de perturbações psiquiátricas ou neurológicas, ou outras patologias com impacto na cognição; g) ausência de medicação susceptível de alterar a função cognitiva; h) ausência de défices motores, visuais ou auditivos significativos, susceptíveis de influenciar o desempenho nas provas; i) ausência de história de alcoolismo ou consumo de substâncias. Os resultados são sugestivos de adequada consistência interna do teste (α Cronbach = .71) e as boas correlações inter-item (superiores entre os itens que constituem um

determinado domínio do MoCA) e item-total [à excepção de dois itens, onde a amostra normativa obteve uma taxa de acertos mais elevada, correspondentes às tarefas de atenção sustentada (.95 ± .219; pontuação máxima de 1 ponto) e de orientação (5.91 ± .396; pontuação máxima de 6 pontos), todos as outras tarefas obtiveram correlações entre .44 e .60 (p < .01) com o total do teste] são indicativas de validade interna. Os resultados no MoCA e no MMSE apresentaram uma boa correlação (r = .66, p < .01), o que evidencia a existência de validade concorrente. A correlação com os resultados na GDS (r = -.33, p < .01) foi sugestiva de validade à semelhança da observada noutros estudos (e.g., Borges, Benedetti & Mazo, 2007).

Simões e colaboradores (2008) realizaram um estudo de validação do MoCA com recurso a três grupos: I) Controlo (critérios de inclusão: função cognitiva global normal, independência funcional e comportamento social adequado), II) DCL (critérios diagnósticos: Petersen, 2004) e III) Demência Ligeira (critérios diagnósticos: queixas mnésicas, confirmadas pelo cuidador e por testes de avaliação neuropsicológica; défices cognitivos que incluem afasia, apraxia, agnosia e/ou perturbação na capacidade de execução; e impacto significativo dos défices na vida social e ocupacional do idoso). O protocolo de avaliação incluía o MoCA, o MMSE e as Matrizes Progressivas Coloridas de Raven (MPCR). Os valores de precisão teste-reteste encontrados foram: MoCA r = .85 [p < .001; 33.47 (± 14.65) dias]; MMSE r = .65 [p < .001; ± 37.0 dias]; MPCR r = .73 [p < .001; 36.47 (± 14.33) dias]. Quanto à consistência interna dos instrumentos, os valores do α Cronbach foram: MoCA α = .92; MMSE α = .87; MPCR α = .92. Ao nível da validade concorrente, os resultados no MoCA apresentaram boas correlações com os do MMSE (r = .83, p < .001) e com os das MPCR (r = .78, p <.001).

Noutro estudo, Duro (2008)[1] procedeu ao exame da validade discriminante dos resultados no MoCA, considerando os seguintes grupos: DCL (n = 82), DA (n = 70), Outras Demências Degenerativas (ODD) (n = 35) e Demência Vascular (DV) (n = 25). Para além de corroborar os dados

anteriores relativos às boas propriedades psicométricas do teste (α Cronbach = .90), o estudo constata uma boa validade discriminativa das pontuações, tendo-se observado diferenças significativas entre os quatro grupos clínicos [($F_{(3,208)}$ = 45.619, $p \leq .001$); por ordem decrescente de desempenho: DCL (19.62 ± 5.49), DV (13.48 ± 5.35), ODD (11.14 ± 5.27) e, com o pior desempenho, DA (10.23 ± 5.07); de acordo com os testes *post-hoc*, as diferenças estatisticamente significativas ocorrem entre os grupos DCL e DA (I.C. 95%:]7,16; 11,63[, $p \leq .001$), DCL e DV (I.C. 95%:]3,01; 9,28[, $p \leq .001$), DCL e ODD (I.C. 95%:]5,71; 11,25[, $p \leq .001$) e DV e DA (I.C. 95%:]0,05; 6,45[, $p < .05$)]. Neste estudo, considerando o ponto de corte original de 26 pontos, o MoCA demonstrou uma sensibilidade de 84.1% na detecção de DCL e 100% para Demência, contra os modestos valores do MMSE (9.9% para DCL e 56.2% para Demência). As correlações entre o MoCA e os outros instrumentos foram elevadas [MMSE r = .82; ADAS-Cog r = -.76], corroborando, uma vez mais, a validade concorrente dos seus resultados.

A identificação da estrutura factorial da versão experimental do MoCA (Duro, Simões, Ponciano & Santana, 2009)[1], com recurso à Análise Factorial Confirmatória (ACF), realizada a uma amostra clínica de 212 pacientes com DCL ou Demência, sugere um modelo com uma estrutura de dois factores, com índices de ajustamento muito bons: um Factor "Memória", que envolve as tarefas de Memória, Linguagem e Orientação (estando esta última mais estreitamente relacionada com a dimensão Memória); e um segundo Factor, denominado "Atenção/Funções Executivas", composto pelas tarefas de Atenção, Concentração e Memória de Trabalho, Funções

[1] Critérios diagnósticos para a constituição dos grupos: a) DCL: Petersen e colaboradores (1999) e de acordo com as *guidelines* internacionais para o diagnóstico de DCL (Petersen, 2007); b) DA: DSM-IV-TR (APA, 2000) e *National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders Association* (McKhann et al., 1984); c) grupo ODD: Consenso para a Degeneração Lobar Frontotemporal (Neary et al., 1998) e Consórcio Internacional para a Demência com Corpos de Lewy (McKeith et al., 2005); d) DV: *National Institute of Neurologic Disorders and Stroke – Association Internationale pour la Recherche et l'Enseignement en Neurosciences* (Roman et al., 1993).

Executivas e Capacidades Visuo-espaciais. A capacidade discriminativa desta estrutura factorial foi explorada, obtendo-se dois resultados principais: 1) ambos os factores discriminam entre DCL e Demência; 2) o factor "Memória" permite discriminar os sujeitos com DA e DV. Atendendo ao segundo resultado referido, os autores deixam em aberto a possibilidade de os resultados no MoCA diferenciarem patologia degenerativa primária (nomeadamente DA) de patologia de etiologia vascular, hipótese cuja comprovação requer, no entanto, a realização de mais estudos.

Fase 4: Meta-análise do Instrumento e do Manual

Paralelamente aos estudos supracitados, o teste e o respectivo manual de administração e cotação foram objecto de sucessivas análises e aperfeiçoamentos pela equipa responsável pelos estudos portugueses com o MoCA.

Numa fase inicial da aplicação à população portuguesa da Versão Experimental do MoCA, foram solicitados a todos os participantes comentários e relatos de quaisquer dificuldades tidas na compreensão das instruções das tarefas. Para além disso, reuniu-se o conjunto de psicólogos com formação/treino e experiência na aplicação do teste para examinar as dificuldades sentidas ao nível das instruções de administração e cotação dos itens. Uma vez identificadas as dificuldades mais frequentes, procedeu-se a uma revisão do manual com o objectivo de aumentar a compreensibilidade das instruções e a clareza dos procedimentos de administração e cotação.

Questões pontuais foram sempre esclarecidas junto dos autores do instrumento original e as alterações efectuadas ao teste e respectivo manual foram debatidas com estes, procurando-se sempre minimizar as diferenças entre a versão original e a Versão Final Portuguesa. Neste processo de adaptação do MoCA, foi igualmente útil a análise das versões existentes noutros países, com realidades culturais e geográficas mais

próximas da Portuguesa, nomeadamente, Espanha, Itália, França e Brasil (cf. www.mocatest.org).

Vejamos, de seguida, as alterações introduzidas no teste e no manual.

A) Alterações efectuadas ao teste

A.1) Alteração da lista de palavras da tarefa de Memória

A lista de palavras que constava da Versão Experimental Portuguesa resultou da tradução das palavras da versão original do MoCA. Ainda que as palavras traduzidas respeitassem os critérios tidos em conta pelos autores para a selecção das palavras na língua inglesa (frequência de uso intermédia, ligeira a média complexidade, culturalmente aceites), verificou-se que: i) a extensão das palavras não era equivalente (e.g., "red" é uma palavra monossilábica, ao passo que "vermelho" é uma palavra trissilábica); ii) na lista de palavras traduzida ocorria repetição fonológica, o que não ocorria na versão inglesa (e.g., veludo e vermelho); e iii) algumas palavras traduzidas apresentavam início silábico idêntico, o que também não sucedia na versão original (e.g., veludo e vermelho). Acresce ainda que Martins (2007) apontou as palavras "malmequer" e "vermelho" como possuindo um menor índice de discriminação. Deste modo, procurando respeitar os critérios originais de selecção das palavras, superar as diferenças supracitadas, manter a equivalência semântica e evitar palavras polissémicas, ponderaram-se várias alternativas, tendo a lista final de palavras sido avalizada por um especialista em Linguística, para assegurar que constituía a melhor opção.

A.2) Alteração das frases para repetição

De modo similar, as frases presentes na Versão Experimental do MoCA resultaram da tradução das frases incluídas na versão original do instrumento. Os critérios tidos em conta pelos autores para a selecção das frases foram: i) complexidade moderada; ii) culturalmente aceites; e iii) conterem entre 7 e 11 palavras (idealmente 9). A frase 2 da Versão

Experimental Portuguesa não cumpria o critério de extensão mencionado pelos autores, sendo constituída por 13 palavras. Tal facto pode justificar a menor correlação deste item com o total da prova, encontrado por Martins (2007). Com o contributo de um especialista em Linguística, ambas as frases foram alteradas, no sentido de cumprirem o critério da extensão da frase (em termos de palavras gramaticais e de grupos acentuais), mantendo, contudo, uma boa fluência e um valor semântico similar ao das frases em inglês presentes na prova original.

B) Alterações efectuadas ao manual

O manual do MoCA contempla as instruções para a administração das tarefas e os critérios para a cotação dos itens. No que diz respeito às instruções fornecidas aos indivíduos, foram realizados sucessivos aperfeiçoamentos entre a Versão Experimental e a Versão Final do manual, que visaram sempre uma maior compreensibilidade e adequação à realidade cultural portuguesa (e.g. palavras exemplo incluídas na instrução da tarefa de fluência verbal).

As instruções de cotação da Versão Final do Manual são mais compreensíveis e objectivas, incluindo mais exemplos e clarificando aspectos não expressos na versão original do manual, que foram esclarecidos junto dos autores da prova. De salientar que para a tarefa de "Subtracção em série de 7" se apresentavam critérios pouco específicos que deixavam margem a alguma subjectividade (e.g. penalizar ou não a pontuação por: recurso a estratégias como contar pelos dedos, relembrar valor da última subtracção efectuada, relembrar o valor a subtrair). Deste modo, foi considerada oportuna uma maior especificação dos critérios de cotação, tendo sido consultados, para esse efeito, diversos especialistas em avaliação neuropsicológica[2].

[2] Agradecimentos: Professor Alexandre Mendonça, Professora Isabel Pavão Martins, Professora Manuela Guerreiro, Professor Óscar Ribeiro, Professora Rosa Novo e Professora Salomé Pinho.

RESULTADOS E DISCUSSÃO

Em Portugal, a escassez de instrumentos objectivos para a avaliação neuropsicológica do défice cognitivo é significativa. Tal realidade acarreta consequências, quer ao nível do diagnóstico e detecção precoce do défice cognitivo, quer na elaboração de planos de intervenção, podendo comprometer o rigor e eficácia da actividade clínica.

Uma forma de amenizar este problema é adaptar instrumentos já disponíveis noutras línguas e utilizados com distintas populações, ao invés de criar novos instrumentos. Com longa história na avaliação psicológica, esta prática tem vindo a aumentar nos últimos anos. Para além de serem, assim, já conhecidos resultados da utilidade e validade dos instrumentos em causa, tal procedimento é susceptível de contribuir para a realização de estudos transculturais, que podem permitir um melhor conhecimento acerca dos quadros clínicos e suas especificidades nas diferentes populações (Cook & Schmitt-Cascallar, 2005; Giusti & Befi-Lopes, 2008).

Não obstante, é frequente que o processo de adaptação de um teste para outra língua sofra a influência de diversas fontes de erro, pelo que é essencial que esse processo adopte procedimentos metodológicos rigorosos. Neste contexto, a tradução e adaptação de um instrumento reveste-se de uma importância similar à da construção de um novo instrumento. A procura do máximo de equivalência entre o instrumento original e a versão traduzida deve conduzir todo o processo, de modo a evitar formas, muitas vezes subtis, de distorção (Giusti & Befi-Lopes, 2008; Hambleton, 2005; Hill & Hill, 2005; International Test Commission, 2001).

A utilização de um instrumento numa determinada população sem a conveniente adaptação coloca em risco a validade e precisão dos resultados. Apesar da importância de todo este processo, é muito rara a referência explícita e detalhada aos procedimentos e análises envolvidas na adaptação dos instrumentos.

O processo de adaptação do MoCA para a população portuguesa, descrito neste trabalho, procurou seguir as linhas orientadoras propostas na

literatura (Hambleton & Patsula, 1999; Hambleton, 2005; Herdman, Fox-Rushby & Badia, 1998; Hill & Hill, 2005; International Test Commission, 2001; Vijver & Poortinga, 2005): tradução, retroversão, realização das correcções necessárias na primeira adaptação linguística do instrumento, estudos com a primeira versão resultante da adaptação, aplicação do teste a uma amostra representativa das populações alvo, análise das características psicométricas do instrumento na nova população, revisão e ajustamentos necessários para finalizar a versão do instrumento, e análise da equivalência entre a versão original e a versão adaptada.

Quanto à questão da equivalência entre o instrumento original e a versão adaptada, Herdman e colaboradores (1998) apresentaram um modelo de avaliação da equivalência da adaptação transcultural de instrumentos, que tem vindo a ser empregue em diversos estudos internacionais. Os autores consideram que a equivalência deve ser avaliada a seis níveis: conceptual, de item, semântica, operacional, de mensuração e funcional, tendo operacionalizado as estratégias de avaliação para cada um dos níveis. Atendendo a este modelo, é possível averiguarmos que o processo de adaptação do MoCA para a população portuguesa respeitou os diferentes níveis apontados, pelo que se pode concluir que a Versão Final Portuguesa do MoCA apresenta equivalência com a versão original do instrumento.

CONCLUSÃO E CONSIDERAÇÕES FINAIS

A Versão Final Portuguesa do MoCA resulta de um longo processo de adaptação transcultural, que procurou ser o mais rigoroso possível, de forma a maximizar a sua adequação à realidade portuguesa, mantendo, ao mesmo tempo, a equivalência com a versão original. Deste complexo processo resulta um teste melhor adaptado para o rastreio cognitivo da população portuguesa, o que se reveste de especial importância, num contexto de escassez de instrumentos de avaliação neuropsicológica devidamente adaptados e validados.

Os estudos com a população portuguesa, aqui descritos, demonstram que o MoCA possui boas qualidades psicométricas, incluindo indicadores de validade e utilidade diagnóstica, discriminando os desempenhos de indivíduos cognitivamente saudáveis ou com envelhecimento normativo dos quadros clínicos de DCL ou DA ligeira e moderada. São necessários mais estudos para averiguar a utilidade do MoCA na diferenciação entre diferentes tipos de demência. Contudo, os resultados preliminares são bastante promissores.

Embora constitua um importante parâmetro no processo de validação de um instrumento, a adaptação transcultural e a avaliação da equivalência são apenas o primeiro passo.

O MoCA é presentemente objecto central de um programa sistemático de trabalhos que inclui os seguintes estudos: 1) Estudo normativo para a população portuguesa (Freitas, Simões, Alves & Santana, 2010, Junho); 2) Estudos psicométricos no âmbito da validade concorrente e precisão (Freitas et al., 2009, Junho); 3) Estudos de validação clínica e exploração da capacidade diagnóstica: DCL, DA, DV, Demência Frontotemporal, Demência com Corpos de Lewy (Freitas, Simões & Santana, 2010, Fevereiro); 4) Estudo longitudinal com pacientes com DCL e DA (Freitas, Santana & Simões, 2010, Julho); 5) Análise dos itens com recurso à Teoria de Resposta ao Item (TRI); 6) Análise da estrutura factorial do MoCA em grupos clínicos e normativos.

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ESTUDO II

Montreal Cognitive Assessment (MoCA): Influence of sociodemographic and health variables

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Abstract

The *Montreal Cognitive Assessment* (MoCA) is a brief cognitive instrument for screening milder forms of cognitive impairment. The present study aimed to analyse the influence of sociodemographic (age, gender, educational level, marital and employment status, geographic region, geographic localisation, and residence area) and health variables (subjective memory complaints of the participant and evaluated by the informant, depressive symptoms and family history of dementia) on the participants' performance on the MoCA. The investigation was carried out in a Portuguese community-based sample of 650 cognitively healthy adults, who were representative of the distribution observed in the Portuguese population. Educational level and age significantly contributed to the prediction of the MoCA scores, explaining 49% of the variance. Regarding health variables, only the subjective memory complaints of the participant showed a small contribution (9%) to the variance on the MoCA scores. This study contributes a useful approach to understanding MoCA performance, stressing the great impact of education and age on scores.

Keywords: Assessment; Elderly; Norms; Mild Cognitive Impairment; Alzheimer´s Disease; Dementia.

INTRODUTION

Several studies have demonstrated that performance on screening tests is influenced by sociodemographic variables. It has been widely reported that age and educational level have a significant effect on cognitive screening test performance. With regard to age, older age has been found to significantly increase the probability of obtaining lower scores (Bravo & Hébert, 1997; Gallacher et al., 1999; Han et al., 2008; Langa et al., 2009; Matallana et al., 2011; Mathuranath et al., 2007; Moraes et al., 2010; Rossetti et al., 2011). Regarding educational level, the worst performance has been found among those with lower educational levels, and ceiling effects have been observed among highly educated individuals. The magnitude of this effect is strong; therefore, education is invariably considered a criterion for the establishment of normative data for cognitive tests (Bravo & Hébert, 1997; Guerreiro et al., 1994; Han et al., 2008; Lieberman et al., 1999; Mathuranath et al., 2007; Measso et al., 1993; Moraes et al., 2010; Morgado et al., 2010; Nguyen et al., 2002; Rossetti et al., 2011). The results regarding gender are more controversial. Some studies have suggested that gender contributes significantly to the explanation of variance on scores of cognitive screening tests (Han et al., 2008; Measso et al., 1993; Mías et al., 2007; Ribeiro et al., 2010; Scazufca et al., 2009), whereas others have not supported this hypothesis (Bertolucci et al., 2001; Lieberman et al., 1999; Mathuranath et al., 2007; Morgado et al., 2010). There has also been a lack of consensus regarding marital status, as some studies have reported greater performances among married persons (Fratiglioni et al., 2000; Moraes et al., 2010; Nguyen et al., 2002; Ribeiro et al., 2010; Wu et al., 2011) while others have found no influence on cognitive state assessment (Bertolucci et al., 2001; Mías et al., 2007). Information regarding employment status is relatively scarce. One study found better scores among individuals who are currently employed (Moraes et al., 2010) and another reported worse scores among individuals with occupations with low intellectual demands (Anderson et al., 2007).

Investigations of geographic variables are complicated and international inter-study comparison is meaningless due to the specificities of the populations and territories. Some research has reported an IQ discrepancy in different geographical regions of a country (Lynn, 1979; Kaufman, McCLean, & Reynolds, 1988), which could be associated with average regional incomes (McDaniel, 2006; Almeida, Lemos, & Lynn, unpublished manuscript). Because there are no Portuguese studies on the influence of geographic variables on cognitive test performance, the inclusion of these variables in the current study assume an exploratory nature.

The influence of health variables on performance at this level of cognitive screening has also been reported in the literature. Co-morbidity of depressive symptoms and cognitive decline is common, and several studies have aimed to clarify the complex interaction between these conditions (Chen et al., 1999; Emery & Oxman, 1992; Rovner et al., 1989). The general tendency toward a poor cognitive performance in the presence of depressive symptoms is well-documented in the literature (Gallacher et al., 1999; Moraes et al., 2010; Nguyen et al., 2002). The manifestation of subjective memory complaints is one of the diagnostic criteria for Mild Cognitive Impairment (Petersen, 2000; Petersen, 2007), but such complaints are also frequent among healthy elderly populations (Reid & MacLullich, 2006). Additionally, also there is a significant association between anxiety and depressive disorders, which further raises questions about the complex relationship between affective symptoms and memory. Reviewing the literature on the influence of subjective memory complaints on cognitive tests and their predictive value of conversion to dementia is a complex task due to the diversity of methodologies used to evaluate subjective memory complaints and cognitive function. As expected, the results of this research are conflicting. Whereas some studies have reported worse performance on cognitive tests among subjects with memory complaints, other investigations have evidenced that memory complaints are a poor indicator of cognitive function (Reid & MacLullich, 2006). Family history of dementia is a well-

known risk factor for Alzheimer's disease; however, few studies have examined the influence of this genetic trait on the cognitive screening tests of healthy subjects. The limited evidence that is available points to a lack of association between these variables (Mías et al., 2007).

The *Montreal Cognitive Assessment* (MoCA; Nasreddine et al., 2005) is a recent screening test that was specifically developed to screen for milder forms of cognitive impairment. Although it was initially designed to assess the cognitive states of patients with Mild Cognitive Impairment and Alzheimer's disease, the MoCA is now an extensively validated screening tool for many disorders (e.g., Parkinson's disease, Huntington's disease, HIV, multiple sclerosis). This measure overcomes the limitations of the *Mini-Mental State Examination* (MMSE; Folstein et al., 1975) because it allows a more comprehensive assessment of the major cognitive domains, including the executive functions assessment, and utilises more complex tasks to measure short-term memory (and with longer delay), language, attention, concentration, working memory, and visuospatial skills. Several studies have reported the good psychometric properties and excellent sensitivity of the MoCA to cognitive impairment, which has driven its rapid international dissemination and recommendation as a cognitive screening tool in various guidelines (Arnold et al., 2007; Chertkow et al., 2007; Hachinski et al., 2006; Gauthier et al., 2011; Ismail et al., 2009; Jacova et al., 2007; Lonie et al., 2009; Zhao et al., 2011). To expand upon this research, new population studies are needed to explore the modulation of MoCA scores by the most significant sociodemographic and health variables, as this analysis has not been done in detail in any country.

Studies of the translation, adaptation, validation, and normative of the MoCA for the Portuguese population were performed by our group (Simões et al., 2008; Freitas et al., 2010a; Freitas et al., 2010b; Freitas et al., 2011). In the present investigation, we aim to analyse the influence of sociodemographic variables (age, gender, educational level, marital status, employment status, geographic region, geographic localization, and

residence area) and health variables (depressive symptoms, subjective memory complaints, and family history of dementia) on the participants' performance on the MoCA using a large Portuguese community-based sample, stratified according to the main sociodemographic variables of the population.

METHODS

Participants and Procedures

The investigation was carried out in a community-based sample of volunteers who were recruited at national health and social security services and resided in all geographic regions of the Portuguese continental territory. This sample is representative of the Portuguese population and was used in a recent MoCA normative study published by our group (Freitas et al., 2011). The inclusion criteria were as follows: age 25 years and older; native speaker of Portuguese and schooling in Portugal; and the absence of significant motor, visual or auditory deficits, all of which may influence performance on tests. To ensure that participants were cognitively healthy adults, we also defined the following exclusion criteria: evidence of loss of autonomy in daily living activities; history of alcoholism or substance abuse; relevant neurological or psychiatric diseases or chronic unstable systemic disorders that impact cognition; significant depressive complaints; and medication with a possible impact on cognition (e.g., psychotropic or psycho-active drugs). A psychologist confirmed these general criteria in an interview that included a complete sociodemographic questionnaire, an inventory of current clinical health status, and past habits and medical history. For older participants, this information was also confirmed by a general practitioner, community centre directors and/or an informant, typically an individual in co-habitation or a close relative.

After this initial selection, all subjects were required to display normal performance on the assessment battery used in this study (see "Materials"), considering the Portuguese cut-off points, for effective inclusion in the study.

Each participant was assessed in a single session by one of two psychologists with expertise in neuropsychological assessment.

From the initial community-based sample of 936 volunteers, 194 subjects (20.73%) were excluded in light of data collected in the interview (most frequent reasons: history of neurological or psychiatric disorder, history of alcohol abuse, and subjective self-evaluation that memory complaints significantly influence day-to-day activities), 58 subjects (6.20%) were excluded due to the presence of significant depressive symptoms (according to the criteria: GDS score over 20 points), and 34 subjects (3.63%) were excluded due to suspected cognitive impairment based on their performance on the assessment battery and respective Portuguese cut-off points.

Only the subjects who met all of the defined inclusion and exclusion criteria were eligible for the study. The final sample comprised 650 cognitively healthy adults, and stratification according to the sociodemographic variables confirmed that this sample was representative of the distribution observed in the Portuguese population (Table 1).

Due to the extensive use of the MoCA in clinical populations, we also established normative data for people 25 years old to allow the use of this instrument with younger patients with other diseases.

Informed consent was obtained from all of the participants after the aims and the procedures of the investigation and confidentiality requirements were fully explained by a member of the study group. The present research complied with the ethical guidelines for human experimentation stated in the Declaration of Helsinki and was approved by the Portuguese Foundation for Science and Technology and by the Faculty of Psychology and Educational Sciences Scientific Committee.

Materials

The assessment battery for the global assessment of each participant was composed of the following instruments:

a) Complete sociodemographic questionnaire.
b) Inventory of current clinical health status.
c) Inventory of past habits and medical history.
d) *Montreal Cognitive Assessment* (MoCA; Nasreddine et al., 2005; Simões et al., 2008), which is a brief cognitive screening instrument that was developed for the screening of milder forms of cognitive impairment. The tool is a one-page test with paper-and-pencil format, and the application time is approximately 10 to 15 minutes. A manual provides explicit instructions for administration and an objectively defined scoring system. The maximum score is 30 points, with higher scores indicating better cognitive performance. It evaluates the following eight cognitive domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration and working memory; and temporal and spatial orientation. In the current study, the MoCA was not used as a diagnostic tool. Furthermore, the MoCA total score refers to the raw score without the correction point for educational effects proposed in the original study (Nasreddine et al., 2005) because this correction point is not used in the Portuguese population (Freitas et al., 2011).
e) *Mini-Mental State Examination* (MMSE; Folstein et al., 1975; Guerreiro et al., 1994), which is the most widely used brief screening instrument for detecting cognitive deficits and, therefore, is not described in detail here.
f) *Clinical Dementia Rating scale* (CDR; Hughes et al., 1982; Garret et al., 2008), which is a global staging tool for dementia that is based on the assessment of cognitive function and functional capacity (in six cognitive-behavioural categories: memory; orientation; sense and problem solving; community activities; home activities and hobbies; and personal care). The scale is administered to the adult/elderly patients and an informant through a semi-structured interview. The CDR was only administered to participants over 49 years of age and when a close informant was available. In the current study, a global score of zero was used as a criterion for inclusion.

g) *Irregular Word Reading Test* (TeLPI: Teste de Leitura de Palavras Irregulares; Alves et al., 2009), which is a tool for estimating premorbid intelligence that consists of a list of 46 irregular words that the participant reads.

h) *Geriatric Depression Scale* (GDS-30; Yesavage et al., 1983; Barreto et al., 2008), which is a brief scale to assess depressive symptoms in adults. It is composed of 30 dichotomous response questions that assess emotional and behavioural symptoms of depression (score range = [0-30]).

i) *Subjective Memory Complaints scale* (SMC; Schmand et al., 1996; Ginó et al., 2008). This scale consists of 10 multiple choice items that assess the presence of subjective memory complaints (score range = [0-21]). It was administered under two conditions: i) SMC-participants: answered by the participants to evaluate their own subjective memory complaints, and ii) SMC-informants: answered by informants to assess their opinion about the memory capacity of the participant (when a close informant was available).

Variable Definitions and Sample Stratification

To enhance the representativeness of the observed distribution in the Portuguese population, the sample of 650 participants was stratified according to the following sociodemographic variables:

I. **age** [age intervals were: 25 – 49 ("young adults": mean age = 38.12 ± 8.086), 50 – 64 ("adults": mean age = 57.12 ± 4.199), and 65 and over ("elderly": mean age = 71.96 ± 5.433)];

II. **gender** [female and male];

III. **educational level** [four educational levels were considered, according to the number of school years successfully completed in the Portuguese education system: 1-4 (primary education), 5-9 (middle school), 10-12 (high school) and over 12 years of education (university/college); these categories match the divisions in the Portuguese school system];

IV. **geographic region** [Portuguese continental territory is divided into five geographic regions (NUTS-II classification; INE, 2010): North, Centre, Lisbon, Alentejo and Algarve];

V. **geographic localization** [two geographic localizations were considered: coast and inland];

VI. **residence area** [according to the Types of Urban Areas (INE, 2010), categorised into predominantly urban areas (PUA), moderately urban areas (MUA) and predominantly rural areas (PRA)].

In this study, we also included the following sociodemographic and health variables that were not criteria for sample stratification:

VII. **marital status** [categorised into “single” (single, divorced or widowed participants) or “married” (married or living in union participants)];

VIII. **employment status** [categorised into “active” (participants with an active work situation) or "inactive" (participants unemployed, retired, or domestic)];

IX. **family history of dementia** [only the information about first-degree relatives was considered relevant, and classification was dichotomised into "positive" or "negative"];

X. **depressive symptoms** [operationalized by the total score on the GDS-30]. Once the participants with severe depressive symptoms were excluded, this study analysed the influence of depressive symptom levels among non-depressed to mildly-depressed individuals on MoCA performance;

XI. **subjective memory complaints** [operationalized by the total score on SMC; two conditions were considered: i) SMC-participants and ii) SMC-informants].

Statistical Analysis

All data analyses were conducted using the *Statistical Package for the Social Sciences*, version 17.0 (SPSS, v.17.0). Descriptive statistics were computed for all sociodemographic and health variables. The observed correlations (using the Pearson correlation coefficient; Cohen, 1988), Cronbach's alpha coefficients, and corrected correlations among measures were also calculated. The differences on the MoCA scores among subgroups stratified according to sociodemographic variables were examined using Student's *t*-test, analysis of variance (ANOVA), *Tukey's* HSD, the *Bonferroni post-hoc* test, and analysis of covariance (ANCOVA). Partial eta squared (η_p^2) was used as an estimate of the effect size (Cohen, 1988). The contribution of the variables age and educational level was the subject of further statistical analysis. The correlation between MoCA scores, age and education was performed using the Pearson correlation coefficient (*r*) (Cohen, 1988). To investigate the significance of age (in years) and education (years of schooling successfully completed) as influencing factors of the MoCA, Multiple Linear Regression (MLR) analyses were performed using the enter method. The multicollinearity was examined through Tolerance and Variance Inflation Factor (VIF) statistics (Meyers et al., 2006), and the coefficient of determination (R^2) was considered in the analysis of effect size in the regressions (Cohen, 1988). Finally, the influence of health variables on the MoCA performance was investigated using MLR analysis, stepwise method, for variables with significant Pearson correlations. All data for this investigation were collected by two neuropsychologists only, which allowed rigorous data collection and procedures. Therefore, the only variable with missing data was SMC-informants, as not all participants had a close informant available (n = 156; 24%). For this variable, the results correspond to 494 participants who had a close informant available.

RESULTS

The final study sample included 650 cognitively healthy participants (mean age = 55.84 ± 15.12, age range = [25-91]; mean education = 8.16 ± 4.72, education range = [2-27]). The sociodemographic characteristics of the sample are presented in detail in Table 3, taking into account the stratification variables as well as the other sociodemographic variables considered in the study. The distribution of the study sample in several strata is comparable to the distribution of the target Portuguese population.

The observed correlations, Cronbach's alpha coefficients, and corrected correlations among the different measures are presented in Table 4. Table 5 summarises the analysis of differences of the MoCA mean scores between the subgroups.

The sociodemographic variables that showed significant group differences (age, educational level, geographic region, area of residence, marital status, and employment status) were targeted for further data analysis. Significant differences in mean age and mean educational level between the subgroups were verified (Table 6). Based on this result, we proceeded with the analysis of covariance to examine whether differences in the MoCA scores remained significant after controlling for the effect of covariates (age and/or educational level) and to estimate the effect size of each variable (Table 7).

The results indicated that after controlling for the effects of covariates, only the variables age, educational level and geographic region contributed significantly to the explanation of variance of the MoCA scores. In the subsequent analysis, we only considered variables whose effect size was medium (age: $F_{(2,646)} = 34.098$, $p < .001$, $\eta_p^2 = .095$) or large (educational level: $F_{(3,645)} = 117.459$, $p < .001$, $\eta_p^2 = .353$). The variable geographic region revealed a small effect size ($F_{(4,643)} = 4.972$, $p = .030$) and, therefore, was not further examined.

Table 3. Sociodemographic characterization n and stratification of the sampl

Variables	Levels	Sample *n* (%)	Portugal *n* (%)
Sociodemographic stratification of sample			
Age	25 - 49	214 (33.0)	-
	50 - 64	218 (33.5)	-
	≥ 65	218 (33.5)	-
Gender	Female	408 (62.8)	3 946 (52.6)
	Male	242 (37.2)	3 559 (47.4)
Educational Level	Primary	256 (39.4)	2 426 (36.6)
	Middle	170 (26.2)	2 280 (34.4)
	High	112 (17.2)	960 (14.5)
	University	112 (17.2)	956 (14.5)
Geographic Region	North	251 (38.6)	2 722 (36)
	Center	174 (26.8)	1 794 (24)
	Lisbon	164 (25.2)	2 091 (28)
	Alentejo	44 (6.8)	577 (8)
	Algarve	17 (2.6)	321 (4)
Geographic Localization	Coast	546 (84)	6 379 (85)
	Inland	104 (16)	1 126 (15)
Residence Area	PUA	446 (68.6)	5 103 (68)
	MUA	112 (17.2)	1 200 (16)
	PRA	92 (14.2)	1 200 (16)
Others Sociodemographic Variables			
Marital Status	Single	489 (75.2)	-
	Married	161 (24.8)	-
Employment Status	Active	330 (50.8)	-
	Inactive	320 (49.2)	-

Abbreviations: PUA = predominantly urban areas; MUA = moderately urban areas; PRA = predominantly rural areas.

Note: The values (*n*) of the Portuguese population are expressed in thousands and represent data of the resident population in continental Portugal aged over 24 years (Instituto Nacional de Estatística, 2010).

Table 4. Observed correlations, Cronbach's alpha coefficients, and corrected correlations among measures

	MoCA	MMSE	TeLPI	GDS	SMC-P	SMC-I
MoCA	**(.78)**	1.10	.73	.27	.39	.07
MMSE	.65**	**(.45)**	.64	.24	.35	.07
TeLPI	-.62**	-.43**	**(.92)**	.16	.24	.10
GDS	-.22**	-.15**	.14**	**(.86)**	.65	.35
SMC-P	-.31**	-.21**	.21**	.54**	**(.80)**	.42
SMC-I	-.05	-.04	-.08	.28**	.32**	**(.73)**

Abbreviations: MoCA = Montreal Cognitive Assessment; MMSE = Mini Mental State Examination; TeLPI = Irregular Word Reading Test; GDS = Geriatric Depression Scale; SMC-P = Subjective Memory Complaints scale of participant; SMC-I = Subjective Memory Complaints scale of informant.

Note: Alpha coefficients are presented on the diagonal, observed correlations below the diagonal (**p < .01), and correlations corrected for attenuation above the diagonal.

Table 5. Analysis of group differences on the MoCA scores (without control of the effect of covariates)

Variables	**MoCA** *M* ± *SD*	***t* / *F***	***Post-hoc***
Age			
25 - 49	26.98 ± 2.548	$F_{(2,647)}$ = 95.130, p < .001	All groups differ.
50 - 64	24.46 ± 3.432		
≥ 65	22.71 ± 3.668		
Gender			
Female	24.50 ± 3.798	t = 1.80, p = .072	-
Male	25.04 ± 3.419		

(Continuation: Tabela 5)

Variables	MoCA *M* ± *SD*	*t* / *F*	*Post-hoc*
Educational Level			
Primary	21.73 ± 3.185	$F_{(3,646)} = 194.996$, $p < .001$	All groups differ. Significant linear effect: $F = 435.895$, $p < .001$
Middle	25.65 ± 2.501		
High	26.77 ± 2.153		
University	28.04 ± 1.942		
Geographic Region			
A. North	24.22 ± 3.644	$F_{(4,645)} = 8.765$, $p < .001$	A ≠ C, D
B. Center	24.28 ± 3.841		B ≠ C, D
C. Lisbon	25.76 ± 3.395		C ≠ A, B, E
D. Alentejo	26.11 ± 2.713		D ≠ A, B, E
E. Algarve	22.41 ± 3.658		E ≠ C, D
Geographic Localization			
Coast	24.80 ± 3.715	$t = 1.546$, $p = .122$	-
Inland	24.19 ± 3.382		
Residence Area			
PUA	24.93 ± 3.728	$F_{(2,647)} = 4.175$, $p = .016$	PUA ≠ PRA
MUA	24.60 ± 3.362		
PRA	23.73 ± 3.604		
Marital Status			
Married	24.40 ± 3.569	$t = 3.652$, $p = <.001$	-
Single	25.61 ± 3.823		
Employment Status			
Active	26.22 ± 2.988	$t = 11.781$, $p = <.001$	-
Inactive	23.13 ± 3.649		

Abbreviations: PUA = predominantly urban areas; MUA = moderately urban areas; PRA = predominantly rural areas; *M*: mean; *SD*: standard deviation; *t*: Student's *t*-test values; *F*: analysis of variance (ANOVA) values; *Post-hoc*: Tukey HSD and Bonferroni post-hoc test analyses.

Table 6. Analysis of covariates: group differences in mean age and educational level

	Age		**Educational Level**	
Variables	*M* ± *DP*	*t* / *F*	*M* ± *DP*	*t* / *F*
Age				
25 - 49	-	-	10.64 ± 4.688	$F_{(2,647)} = 62.757$, $p < .001$
50 - 64			7.75 ± 4.289	
≥ 65			6.08 ± 3.989	
Educational Level				
Primary	63.99 ± 10.843	$F_{(3,646)} = 57.631$, $p < .001$	-	-
Middle	53.69 ± 14.454			
High	48.69 ± 14.523			
University	47.50 ± 16.008			
Geographic Region				
North	53.53 ± 13.741	$F_{(4,645)} = 6.517$, $p < .001$	6.91 ± 3.891	$F_{(4,645)} = 15.675$, $p < .001$
Center	60.09 ± 14.092		8.50 ± 5.382	
Lisbon	54.41 ± 16.454		10.20 ± 4.627	
Alentejo	54.82 ± 18.746		7.59 ± 4.299	
Algarve	63.12 ± 10.624		4.94 ± 2.703	
Residence Area				
PUA	55.63 ± 14.879	$F_{(2,647)} = 2.094$, $p = .124$	8.60 ± 4.871	$F_{(2,647)} = 8.450$, $p < .001$
MUA	54.43 ± 16.408		7.79 ± 4.298	
PRA	58.62 ± 14.456		6.46 ± 4.064	
Marital Status				
Married	57.24 ± 13.431	$t = 3.527$, $p = .001$	7.65 ± 4.551	$t = 4.842$, $p = <.001$
Single	51.60 ± 18.789		9.70 ± 4.917	
Employment Status				
Active	45.84 ± 11.549	$t = 23.147$, $p = <.001$	9.81 ± 4.739	$t = 9.673$, $p = <.001$
Inactive	66.16 ± 10.829		6.46 ± 4.065	

Abbreviations: *M*: mean; *SD*: standard deviation; *t*: Student's *t*-test values; *F*: analysis of variance (ANOVA) values.

Table 7. Analysis of group differences in the MoCA scores while controlling for the effect of covariates and estimation of the effect sizes

Variables	Covariates	*ANCOVA*	*Effect Size*
Age	Educational level	$F_{(2,646)} = 34.098$, $p < .001$	Medium $\eta_p^2 = .095$
Educational Level	Age	$F_{(3,645)} = 117.459$, $p < .001$	Large $\eta_p^2 = .353$
Geographic Region	Age Educational level	$F_{(4,643)} = 4.972$, $p = .001$	Small $\eta_p^2 = .030$
Residence Area	Educational level	$F_{(2,646)} = .122$, $p = .885$	Null $\eta_p^2 = .000$
Marital Status	Age Educational level	$F_{(1,646)} = .014$, $p = .907$	Null $\eta_p^2 = .000$
Employment Status	Age Educational level	$F_{(1,646)} = 3.469$, $p = .063$	Null $\eta_p^2 = .005$

Abbreviations: *F*: analysis of covariance (ANCOVA) values; η_p^2: partial eta squared value

Note: According to Cohen [44], η_p^2 values of .01, .06 and .14 are considered small, medium and large effect sizes, respectively.

Statistically significant correlations were observed between the MoCA scores and age ($r = -.522$, $p < .01$) and educational level ($r = .652$, $p < .01$). To examine the contributions of these variables and their interactions to the explanation of variance of the MoCA scores, a MLR analysis was performed using the enter method. This analysis resulted in two significant

regression models. The first model ($F_{(1,648)}$ = 480.093, p < .001) included only the variable educational level (β = .652, t = 21.911, p < .001), which significantly explained 42.5% of total variance of the MoCA scores. In the second regression model, the two variables were combined, and no evidence of multicollinearity was detected. In this model ($F_{(2,647)}$ = 317.016, p < .001), both variables significantly contributed to the prediction of the MoCA scores (educational level: β = .524, t = 16.871, p < .001; age: β = -.293, t = -9.426, p < .001). The beta weights indicated that educational level was the major contributor to the prediction of the MoCA scores, but age also contributed to the prediction. The adjusted R squared value was .49, which signifies that 49% of the variance on the MoCA scores was explained by this model.

The health variables considered in the study were as follows: family history of dementia (16% of participants had a positive family history), depressive symptoms (GDS mean = 7.34 ± 5.371, range = [0-20]), and subjective memory complaints [two conditions: i) SMC-participants (mean = 5.66 ± 3.592, range = [0-18]) and ii) SMC-informants (mean = 4.15 ± 2.735, range = [0-11])]. The results of the intercorrelations among the MoCA scores and these health variables are provided in Table 4, except for the family history of dementia, which showed no significant correlation with MoCA scores (r = .00, p < .001) or SMC-informants scores (r = .095, p = .239) and a significant correlation with GDS scores (r = .092, p = .019) and SMC-participants scores (r = .127, p < .01).

We observed that MoCA scores only showed a statistically significant and negative correlation with depressive symptoms and the subjective memory complaints of the participants. The influence of these health variables on MoCA performance was investigated using MLR analysis, stepwise method. The resulting model ($F_{(2,647)}$ = 64.860, p < .001) only included the subjective memory complaints of the participant, which explained 9% of the total variance on the MoCA scores. Depressive

symptoms did not reveal a significant contribution to the model (β = -.082, t = 1.845, p = .065).

DISCUSSION

A reliable evaluation of an individual's cognitive performance must be based on robust normative data stratified according to the sociodemographic variables most influential on and predictive of performance. The current study is essential for adapting this instrument for a specific population. Furthermore, the study is relevant due to the widespread international use of the MoCA, the lack of international studies that analyse a wide variety of variables that may influence one's performance on this test, and the absence of studies using stratified community-based samples in Portugal to examine the influence of sociodemographic and health variables on cognitive screening instruments. The few studies available were limited by small samples within restricted regional areas and only focused on specific variables. The use of a sample stratified by different levels of sociodemographic variables and with a distribution close to that observed in the Portuguese population enhances the equivalence with the target population and the confidence of conclusions drawn.

Our results confirm that age and educational level significantly contribute to the prediction of the MoCA scores, explaining 49% of the results variance. This is considered a large effect, according Cohen (1988), and a respectable result, according to Pallant (2007). As expected, and according to previous studies of cognitive screening tests (Anderson et al., 2007; Bravo & Hébert, 1997; Gallacher et al., 1999; Langa et al., 2009; Matallana et al., 2011; Mathuranath et al., 2007; Moraes et al., 2010), our results confirm that older age and lower educational level have a significant effect on MoCA performance, increasing the likelihood of obtaining a lower total score.

The influence of other sociodemographic variables on screening tests is further conflicting in the literature. In the present study, gender,

marital status, and employment status did not reveal a significant effect on the MoCA results. Regarding geographical variables, our results indicated no statistically significant differences between subjects living in the coastal and inland areas. The differences observed among residents in predominantly urban or rural areas were not significant after controlling for education. Finally, the observed differences between residents in different geographic regions showed a small magnitude after controlling for age and education. Of note, these regional subgroups were not completely matched for age and education, which may explain the results obtained.

Regarding the influence of health variables on MoCA performance, similar to a previous study (Mías et al., 2007), the results suggest no significant association between family history of dementia or memory complaints evaluated by the informant and MoCA performance. On the other hand, both depressive symptoms and subjective memory complaints of the participant presented significant and negative correlations with total MoCA scores. Moreover, these variables also showed a significant correlation between them, which is consistent with the well-documented association between these symptoms (Reid & MacLullich, 2006). However, considering the results of the MLR analysis performed, only the subjective memory complaints of the participant showed a small contribution (9%) to the explanation of the variance on the MoCA scores.

One of the main limitations of the present study was the inability to completely match all of the age-subgroups in terms of education due to the higher education of the younger group. However, the observed discrepancy is, in fact, representative of the demographic profile of the country. This can be explained by the change in the school system in the last decades, namely the imposition of higher levels of obligatory education, which has had a selective impact on the younger generations. The older strata were characterised by a very low mean education. Another issue involves the classification of participants as cognitively healthy subjects. To ensure cognitive health, we established strict criteria for inclusion and exclusion in

the sample, as previously explained, and these criteria were confirmed in the clinical interview and neuropsychological evaluation. Furthermore, for older participants, confirmatory information was also obtained through a general practitioner, community centre directors and/or an informant. However, given the sample size and geographical distribution of the participants, it was not possible to perform a neurological consultation or additional diagnostic tests such as neuroimaging, which would have further ensured the normal cognitive status of participants. In addition, data regarding health variables, such as depressive symptoms and subjective memory complaints, could be better operationalized. The inclusion of more specific and descriptive instruments may have shed greater light on the influence of these variables on MoCA performance. Furthermore, the current findings regarding the effect of depressive symptoms among non-depressed-to-mildly-depressed individuals must be complemented with studies that consider patients with depression. Finally, due to the lack of international studies analysing the influence of sociodemographic and health variables on MoCA performance, there is no comparison for these results.

This study is a useful approach for better understanding MoCA performance in a community population. The influence of education and age on MoCA scores was clearly demonstrated, and therefore, these variables are the optimal criteria for the establishment of MoCA normative data for the Portuguese population.

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ESTUDO III

Construct validity of the Montreal Cognitive Assessment (MoCA)

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Abstract

The *Montreal Cognitive Assessment* (MoCA) is a brief instrument developed for the screening of milder forms of cognitive impairment. The present study aims to assess the construct related validity of the MoCA through the establishment of the factorial, convergent and discriminant related validities, and the reliability of data. In a Portuguese sample of 830 participants, several models were tested using Confirmatory Factor Analysis (CFA). Although all tested models showed a good fit, the six-factor model based on the conceptual model proposed by the MoCA´s authors showed a significantly better fit. The results allowed us to establish the factorial, convergent and discriminant validity of this six-dimensional structure. An overall psychometric adequacy of the items, and a good reliability were also found. This study contributes to overcome an important gap in the construct related validity of this instrument. The present findings corroborate the six-dimensional structure of the MoCA and provide good evidence of the construct related validity. The MoCA has proved to be an appropriate measure for cognitive screening taking into account different cognitive domains, which will enable clinicians and researchers to use this test and its six latent dimensions in order to achieve a better understanding of the individuals' cognitive profile.

Keywords: cognitive disorders; Alzheimer disease; neuropsychological test; psychometrics; validity and reliability; factor analysis.

INTRODUCTION

The *Montreal Cognitive Assessment* (MoCA - Nasreddine, Phillips, Bédirian, Charbonneau, Whitehead, Collin, Cummings & Chertkow, 2005) is one of the most recent screening tests, specifically developed for the screening of milder forms of cognitive impairment. Surpassing the limitations of the *Mini-Mental State Examination* (MMSE – Folstein, Folstein & McHugh, 1975), the MoCA is now recognized as one of the best cognitive screening tests (Appels & Scherder, 2010; Ismail, Rajji & Shulman, 2009; Jacova, Kertesz, Blair, Fisk & Feldman, 2007; Lonie, Tierney & Ebmeier, 2009). Although it was initially designed to assess the cognitive state of patients with Mild Cognitive Impairment and with Alzheimer's disease, currently the MoCA is an extensively validated screening tool for many disorders. Several studies have proved the good psychometric properties and excellent sensitivity of data gathered with the MoCA. Its ability for the early identification of cognitive decline throughout the course of the disease, has promoted its rapid international dissemination (see studies in http://www.mocatest.org). Beyond its screening properties, the MoCA can also be used as a quantitative estimate of the overall cognitive ability (Koski, Xie & Finch, 2009; Koski, Xie & Konsztowicz, 2011), and as an indicator of the global cognitive decline in patients' longitudinal monitoring (Freitas, Santana & Simões, 2010).

Despite its current widespread use and clinical validity studies, the internal structure of the MoCA needs to be studied more systematically. Nasreddine et al. (2005) made a theoretical proposal according to which the MoCA's 30 items could be categorized into the following cognitive domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration and working memory; and temporal and spatial orientation.

Duro et al. (2010) analyzed the dimensions underlying the MoCA in a heterogeneous clinical sample with cognitive decline, not having confirmed

the structure originally suggested by the MoCA authors (Nasreddine et al., 2005). In this study, a two-factor model was found as best solution: the first factor was designated "Memory", it comprised memory, language and orientation tasks; the second factor was designated "Attention / Executive Functions", it included attention, executive functions and visuospatial skills. It should be noted that this study used the MoCA's Portuguese experimental version, while the present study uses the MoCA's Portuguese final version, which resulted of the adaptation process for the Portuguese population and which is significantly different from the first. The main changes occurred at the level of the words of the memory task and sentences for repetition (translated version used in MoCA's Portuguese experimental version was not equivalent with the original version in words and sentences length), as well as in administration and scoring instruction manual (which was improved after the studies conducted with the experimental version), as described by Freitas, Simões et al. (2010). To date, and as far as we know, there have been no other studies on the factorial structure of the MoCA in clinical populations and there aren´t any studies with community samples, which represents an important gap in the construct related validity of this instrument.

Translation, adaptation and validation studies, as well as normative study of the MoCA on the Portuguese population were performed by our research group (Freitas et al., 2010a, 2010b; Freitas, Simões, Alves & Santana, 2011; Simões, Freitas, Santana, Firmino, Martins, Nasreddine & Vilar, 2008). The present study was undertaken to assess the construct related validity of the MoCA. Firstly, we examined the psychometric properties of the items and scale, and then we analyzed the factorial structure of the MoCA and established the respective factorial, convergent and discriminant related validities.

METHODS

Participants and Procedures

The total sample was comprised of 830 participants distributed between two main subgroups:

I) Healthy Group

The healthy group was composed by cognitively healthy community dwellers, living in all geographic regions of the Portuguese continental territory. These individuals were recruited through the national health and social security services. This sample served as the basis for the MoCA normative study for the Portuguese population (Freitas et al., 2011). Several demographic and clinical inclusion criteria were considered in the initial selection phase: individuals 25 years and over; Portuguese as the native language and schooling in Portugal; absence of significant motor, visual or auditory deficits - all of which may influence performance on tests; and to ensure that participants were cognitively healthy adults: autonomy in daily activities; no history of alcoholism or substance abuse; absence of neurological or psychiatric diseases, as well as of chronic unstable systemic disorders with impact in cognition; absence of significant depressive complaints and medication with possible impact in cognition (e.g., psychotropic or psycho-active drugs). The presence of these criteria was confirmed by a psychologist in an interview through a standard questionnaire that included a complete socio-demographic questionnaire, an inventory of current clinical health status, and past habits and medical history. Regarding older participants, this information was also checked with general practitioners, community center directors and/or an informant, usually an individual that lived with the participant or a close relative. After this initial selection, a set of instruments of global assessment was administered to all subjects: a comprehensive sociodemographic questionnaire; an inventory of the current clinical health status, past habits and medical history; the MMSE (Folstein et al., 1975; Guerreiro, 1998); the *Clinical Dementia Rating* scale

(CDR - Hughes, Berg, Danziger, Coben & Martin, 1982; Garret, Santos, Tracana, Barreto, Sobral & Fonseca, 2008), only for participants over 49 years old; the *Irregular Word Reading Test* (TeLPI: Teste de Leitura de Palavras Irregulares - Alves, Simões & Martins, 2009), for pre-morbid intelligence estimation; the *Subjective Memory Complaints* scale (SMC - Schmand, Jonker, Hooijer & Lindeboom, 1996; Ginó, Mendes, Ribeiro, Mendonça, Guerreiro & Garcia, 2008); and the *Geriatric Depression Scale* (GDS-30 - Yesavage, Brink, Rose, Lum, Huang, Adey & Leirer, 1983; Barreto, Leuschner, Santos & Sobral, 2008). The inclusion criteria required each individual to have a normal performance in the aforementioned instruments. Each participant was assessed in a single session by one of the two psychologists with expertise in neuropsychological assessment. From the initial community-based sample of the 936 volunteers, 194 (20.73%) were excluded according to data collected in the interview (the most frequent reasons were: history of neurological or psychiatric disorder and a history of alcohol abuse), and 92 (9.83%) were further excluded due to the presence of significant depressive symptoms, or because the performance on the assessment battery was indicative of cognitive impairment according to the Portuguese cut-off points. The final group is composed of 650 cognitively healthy adults that met all the inclusion and exclusion criteria previously described. Cross tabulation of the participants according to socio-demographic variables reproduced the stratification accordingly to age group, gender, educational level, geographic region, geographic localization and residence area of the Portuguese population (Freitas et al., 2011).

II) Clinical Group

The clinical group included 90 patients with Mild Cognitive Impairment (MCI) and 90 patients with Alzheimer's disease (AD), recruited from the Dementia Clinic, Neurology Department of Coimbra University Hospital. All patients were clinically examined through neurological, biochemical, and image studies - structural (CT and/or MRI) and functional (SPECT and/or PET) – considered to be essential in the exclusion of other

causes and forms of cognitive decline. Furthermore, all patients underwent a comprehensive neuropsychological assessment battery which comprised the following instruments: the MMSE (Folstein et al., 1975; Guerreiro, 1998), the CDR (Hughes et al., 1982; Garret et al., 2008), the *Alzheimer´s Disease Assessment Scale* (ADAS – Rosen, Mohs & Davis, 1984; Guerreiro, Fonseca, Barreto & Garcia, 2008); the TeLPI (Alves et al., 2009), the SMC (Schmand et al., 1996; Ginó et al., 2008), and the GDS-30 (Yesavage et al., 1983; Barreto et al., 2008). Each participant was assessed in a single session by one of two neuropsychologist experts. The diagnoses were previously established through a consensus reached by a multidisciplinary team based on the international criteria for the MCI of the Petersen workgroup (Petersen, 2004) and probable AD (American Psychiatric Association, 2000; McKhann, Drachman, Folstein, Katzman, Price & Stadlan, 1984). The MCI group included patients classified as "amnestic MCI" (single or multidomain) (Petersen, 2007) and with a classification of 0.5 on the CDR. The AD group included only patients with mild to moderate severity (classified with CDR ≤ 2 and MMSE ≥ 12 points). Only the patients with a completed clinical evaluation, a well established diagnosis according to the above international criteria and a stable clinical condition, without significant comorbidities, were eligible for this study. Thirty patients were initially excluded due to the fact that the differential diagnosis had not yet been established by the multidisciplinary team. Also at the outset the exclusion criteria were: high dementia's severity, recent pharmacotherapy changes, recent psychiatric comorbidity (a clinical diagnosis in the 6 months prior to the current neuropsychological evaluation), and significant motor, visual or auditory deficits, all of which may influence in neuropsychological assessment. Additionally, each patient who participated in the study had a diagnosis confirmed by a neurologist at the time of the data collection.

For this study purposes, two control sub-groups were selected from the healthy group in order to match each patient on variables that were found to be predictive of the MoCA´s performance (educational level and

age) (Freitas et al., 2011). These group's subjects were additionally matched on gender. As a result, a perfect match was obtained between the group with MCI and the control group (afterwards named C-MCI group) and between the group with AD and the associated control group (C-AD Group).

An informed consent was obtained from all the participants after the research aims and procedures, as well as the confidentiality requirements, were fully explained by a member of the research team. For the AD patients who were not capable of providing the informed consent, a legal representative fulfilled that requirement on their behalf. The present research complies with the ethical guidelines on human experimentation stated in the Declaration of Helsinki and was approved by the Portuguese Foundation for Science and Technology and by the Faculty of Psychology and Educational Sciences Scientific Committee.

Measure: Montreal Cognitive Assessment

The MoCA is a brief cognitive screening tool, which provides a quick indication of an individual's global cognitive state. It is a tool in paper-and-pencil format, composed by a one-page test, which requires a short administration time, and by a manual explicitly describing the instructions for administering the tasks and objectively portraying the defined scoring system. The MoCA covers a wide range of cognitive functions such as short-term memory, executive functions, visuospatial abilities, language, attention, concentration, working memory, and temporal and spatial orientation. The short-term memory (5 points) is tested by a delayed recall of the five nouns previously learned in two trials. The executive functions (4 points) are evaluated by an alternation task adapted from the Trail Making B task, a phonemic fluency task, and a two verbal abstraction tasks. The visuospatial skills (4 points) are assessed using a three-dimensional cube copy and a clock-drawing task (contour, numbers and hands). The language (5 points) is tested by naming three low-familiarity animals, repeating exactly two syntactically complex sentences, and by the phonemic fluency task above

mentioned. The attention, concentration, and working memory (6 points) are assessed using digits forward and backward, a sustained attention task, and a serial subtraction task. Finally, the time orientation (4 points) is tested by asking the subject the date, month, year, and day; while the space orientation (2 points) is tested by asking the subject in what place and city they are in (Nasreddine et al., 2005). A MoCA score is derived by adding the points of each successfully completed task, in a range from 0 to 30 points, with higher scores indicating better cognitive performance.

Statistical Analyses

Statistical analyses were performed using the *Statistical Package for the Social Sciences* (SPSS, version 19.0) (IBM SPSS, Chicago, IL) and the package *Analysis of Moment Structures* (AMOS version 19.0) (IBM SPSS, Chicago, IL). Descriptive statistics were used for the sample's characterization and analysis of the distribution responses to each item. The χ^2 test and the two-sample *t*-test allowed the establishment of the two groups comparisons. To assess item/domain discriminating power, the Pearson's correlation coefficient was performed between each item and the total score, each item and cognitive domains, and between each cognitive domain and the MoCA total score (Himmelfarb, 1993). Non-significant correlation coefficients indicate lack of factorial validity, while significant correlation coefficients are an indicator of factorial validity. The Cronbach´s alpha is considered as an index of internal consistency. This reliability value should be equal to or higher than 0.7 (Hair, William, Barry, Rolph & Ronald, 2010).

The MoCA's diagnostic accuracy for MCI and AD patients was assessed through the receiver operating characteristics (ROC) curve analysis. In this analysis, the areas under the curve (AUC) can vary between 0.5 and 1, with larger AUC indicating better diagnostic accuracy. The optimal cut-off points were calculated for each group according to the highest

Youden index, with higher Youden index indicating maximization of the sensibility and specificity.

Confirmatory Factor Analysis (CFA) was conducted to provide further evidence to MoCA's construct validity. Since MoCA's items are dichotomic, model estimation was done with tetrachoric correlations and the weighted least squares mean and variance adjusted estimation procedure implemented in Mplus6 (Muthén & Muthén, Los Angeles, CA). To evaluate the goodness of fit of the tested factorial structures the indices χ^2/df, CFI (Comparative Fit Index), TLI (Tucker-Lewis Index), RMSEA (Root Mean Square Error of Approximation) were used. Values indicative of good fit were those generally assumed in CFA (Marôco, 2010, Byrne, 2010): χ^2/df ~ 2-3, CFI and TLI > 0.9; and RMSEA < .05.

RESULTS

Sample Characterization

The total sample was comprised of 830 participants. The characterization of the study sample and in more detail of the all subgroups is presented in Table 8. For this description were considered the following variables: sample size, educational level, age, gender, and MoCA score.

The control participants included in the paired sub-sample were select from the health group in order to match in educational level, age and gender to patients of clinical groups. No statistically significant differences were found on the educational level ($t_{(178)} = .049$, $p = .961$), age ($t_{(178)} = .833$, $p = .406$), and gender ($\chi^2_{(1)} = .000$, $p = 1.0$) between the MCI and the C-MCI group. Likewise, the AD and the C-AD group did not differ on the educational level ($t_{(178)} = .018$, $p = .986$), age ($t_{(178)} = .955$, $p = .341$), and gender ($\chi^2_{(1)} = .000$, $p = 1.0$). The MCI group and the AD group did not differ on educational level ($t_{(178)} = .411$, $p = .681$) and gender ($\chi^2_{(1)} = .092$, $p =$

.761), but nevertheless the AD patients were significantly older than MCI patients ($t_{(178)} = 3.071$, $p = .002$).

Table 8. Descriptive statistics for the total sample and subgroups

	n	Education	Age	Gender	MoCA
Total Sample	830	7.77 ± 4.699	59.43 ± 15.498	515 (62.0)	22.42 ± 6.061
Healthy Group	650	8.16 ± 4.724	55.84 ± 15.120	408 (62.8)	24.70 ± 3.668
Clinical Group	180	6.37 ± 4.338	72.37 ± 8.270	107 (59.4)	14.18 ± 5.851
Paired Sample	360	6.38 ± 4.316	71.86 ± 7.895	214 (59.4)	18.59 ± 6.503
MCI	90	6.50 ± 4.565	70.52 ± 7.950	55 (61.1)	18.31 ± 3.868
C-MCI	90	6.53 ± 4.498	69.59 ± 7.053	55 (61.1)	23.64 ± 3.223
AD	90	6.23 ± 4.119	74.22 ± 8.212	52 (57.8)	10.06 ± 4.410
C-AD	90	6.24 ± 4.128	73.10 ± 7.539	52 (57.8)	22.33 ± 3.471

Abbreviations: MoCA: Montreal Cognitive Assessment (maximum score = 30); MCI: Mild Cognitive Impairment patients; C-MCI: subgroup of controls matched with MCI patients; AD: Alzheimer's Disease patients; C-AD: subgroup of controls matched with AD patients.

Note 1: Health Group: all cognitively health participants; Clinical Group: all patients with MCI and AD; Control Group: cognitively health participants paired with patients; Paired Sample: sum of all the patients and their matched controls.

Note 2: Gender is characterized by female's *n* and respective percentage (%). Data of others variables are presented as mean ± standard deviation.

Item Analysis

To evaluate the distribution responses to each item, the response frequencies were computed (dichotomous items: 0 or 1 point). For the purpose of this analysis we used the paired sample ($n = 360$) in order to balance the proportion of healthy controls and patients and minimize the possible influence of sociodemographic differences. The results are provided in Table 9.

Table 9. Analysis of the distribution responses of the MoCA´s items

Item Code	% Incorrect Answers	% Correct Answers
TMT-B (adapted)	56.7	43.3
Cube	62.2	37.8
Contour	2.2	97.8
Numbers	44.7	55.3
Hands	57.8	42.2
Lion	9.7	90.3
Rhinoceros	57.5	42.5
Camel	18.3	81.7
Digits Forward	45.8	54.2
Digits Backward	30.3	69.7
Sustained Attention	16.9	83.1
Subtraction 1	14.2	85.8
Subtraction 2	51.9	48.1
Subtraction 3	48.1	51.9
Subtraction 4	51.7	48.3
Subtraction 5	55.8	44.2
Sentence 1	29.2	70.8
Sentence 2	52.2	47.8
Phonemic Fluency	73.1	26.9
Abstraction 1	35.8	64.2
Abstraction 2	64.4	35.6
Word 1	68.6	31.4
Word 2	66.7	33.3
Word 3	52.2	47.8
Word 4	70.6	29.4
Word 5	53.3	46.7
Date	26.4	73.6
Month	13.3	86.7
Year	19.4	80.6
Day	12.8	87.2
Place	3.3	96.7
City	0.8	99.2

Note: All values are expressed in percentage (%).

A close examination of these results reveals that the items Contour, Lion, Place and City have a high hit rate (greater than 90%) which suggests a low index of difficulty. On the other hand, Phonemic Fluency is the item with the lower hit rate (26.9%).

The correlations between each item and the total score, and each item and the cognitive domains, as were conceptualized by the authors (Nasreddine et al., 2005), were also explored. As demonstrated in Table 10, each of the 32 items showed a significant ($p < .001$) and positive correlation with the total score of the scale, with lower correlations of Contour, Lion, Place, and City items (respectively .168, .344, .277, .257). These were simultaneously the items with higher hit rate (respectively 97.8, 90.3, 96.7, 99.2). Therefore, these items reveal a lower contribution for the individual information obtained with the MoCA. Regarding the correlation coefficients of each item with the cognitive domains, all the items showed a significantly higher correlation with the respective domain, according to the structure proposed by the authors, as compared to the correlations with any other domain. With the exception of the Contour, Place, and City items, that showed lower correlations with any domain. Although the Contour did not exhibit a differentiated correlation with any domain, the Place and City showed a significantly higher correlation with Orientation than with any of the others domains. Despite the consideration that the Phonemic Fluency contributes to the two domains in the original MoCA formulation, we found a higher correlation with the Executive Functions domain than with the Language domain.

As shown in Table 11, correlations between each cognitive domain and the MoCA total score were high and positive, ranging from .711 to .801. These correlations are suggestive of construct related validity. Furthermore, we can observe that each domain showed significantly higher correlation with the MoCA total score than with another domain, what is suggestive of discriminative power of domains.

Table 10. Correlation coefficients of each item with total score and cognitive domains

Item Code	Total Score	Mem	EF	VSS	Lang	ACWM	Ori
TMT-B (adapted)	.626**	.426**	**.674****	.544**	.384**	.447**	.419**
Cube	.505**	.221**	.491**	**.734****	.348**	.425**	.183**
Contour	.257**	.141**	.139**	.249**	.168**	.216**	.266**
Numbers	.654**	.354**	.555**	**.797****	.448**	.465**	.454**
Hands	.581**	.281**	.507**	**.798****	.382**	.423**	.353**
Lion	.344**	.102	.257**	.283**	**.533****	.178**	.275**
Rhinoceros	.402**	.165**	.326**	.301**	**.682****	.258**	.213**
Camel	.545**	.310**	.394**	.347**	**.672****	.385**	.373**
Digits Forward	.470**	.214**	.308**	.306**	.397**	**.606****	.258**
Digits Backward	.396**	.199**	.272**	.250**	.215**	**.579****	.193**
Sustained Attention	.580**	.369**	.329**	.366**	.380**	**.647****	.483**
Subtraction 1	.498**	.238**	.379**	.357**	.328**	**.604****	.375**
Subtraction 2	.536**	.343**	.395**	.424**	.369**	**.570****	.324**
Subtraction 3	.513**	.281**	.327**	.416**	.319**	**.629****	.331**
Subtraction 4	.485**	.286**	.332**	.357**	.296**	**.612****	.277**
Subtraction 5	.523**	.250**	.371**	.445**	.357**	**.632****	.302**
Sentence 1	.535**	.280**	.365**	.364**	**.624****	.423**	.391**
Sentence 2	.440**	.228**	.274**	.272**	**.607****	.365**	.267**
Phonemic Fluency	.449**	.208**	**.659****	.388**	**.338****	.316**	.206**
Abstraction 1	.467**	.216**	**.635****	.399**	.351**	.349**	.248**
Abstraction 2	.504**	.274**	**.723****	.440**	.338**	.340**	.259**
Word 1	.472**	**.671****	.311**	.238**	.249**	.242**	.323**
Word 2	.503**	**.740****	.284**	.262**	.252**	.278**	.341**
Word 3	.612**	**.756****	.407**	.365**	.307**	.398**	.445**
Word 4	.418**	**.687****	.194**	.183**	.204**	.227**	.314**
Word 5	.584**	**.797****	.334**	.302**	.296**	.392**	.442**
Date	.642**	.473**	.367**	.394**	.393**	.456**	**.820****
Month	.570**	.382**	.300**	.319**	.385**	.390**	**.797****
Year	.673**	.462**	.400**	.424**	.473**	.452**	**.856****
Day	.552**	.370**	.316**	.319**	.345**	.391**	**.763****
Place	.277**	.165**	.136**	.157**	.142**	.198**	**.460****
City	.168**	.099	.073	.052	.163**	.111*	**.267****

Abbreviations: Mem: Short-term Memory; EF: Executive Functions; VSS: Visuospatial skills; Lang: Language; ACWM: Attention, Concentration and Working Memory; Ori: Orientation to time and space.

Note: $^{*}p < .05$; $^{**}p < .001$

Table 11. Correlation coefficients of the cognitive domains and total score

	Total Score	EF	VSS	Lang	Mem	ACWM	Ori
Total Score	-						
EF	.757	-					
VSS	.752	.655	-				
Lang	.767	.638	.549	-			
Mem	.711	.418	.372	.369	-		
ACWM	.801	.537	.569	.552	.427	-	
Ori	.745	.420	.442	.478	.513	.515	-

Abbreviations: EF: Executive Functions; VSS: Visuospatial skills; Lang: Language; Mem: Short-term Memory; ACWM: Attention, Concentration and Working Memory; Ori: Orientation to time and space.

Note: All correlation coefficient were significant at the .001 level.

Scale Reliability

Internal consistency reliability of the MoCA was estimated using Cronbach's α. In the total paired sample (*n* = 360), we found a Cronbach's α of .903 that confirms the overall reliability of the scale when used to examine Portuguese subjects. A more detailed analysis reveals that there is no improvement regarding the reliability coefficient value with the exclusion of any item of the scale. This reliability coefficient was also computed for each sub-group. In the clinical group (*n* = 180) the respective value was .883, while in the control group (*n* = 180) it was .678. In the total sample (*n* = 830) we found a Cronbach's α of .905.

Diagnostic Accuracy

The ROC curve analysis was conducted on paired sample (*n* = 360) to evaluate the diagnostic accuracy of MoCA to discriminate MCI and AD patients from cognitively healthy adult. The discriminant potential of the MoCA for MCI was high, with an AUC of .856 (95% CI = .796 - .904) and for AD was excellent, with an AUC of .980 (95% CI = .947 - .995). According to

the Youden index, the optimal cut-off point for MCI was below 22 points (sensitivity = 81%; specificity = 77%). For the AD patients, the optimal cut-off point was below 17 points (sensitivity =88%; specificity = 98%).

Confirmatory Factor Analysis

I) Model specification

The CFA was performed to provide further evidence of the MoCA's construct validity. Three models were contemplated in the analyses. The first model (a six-factor model) was based on the original conceptual model proposed by the MoCA's authors (Nasreddine et al., 2005). The second model (two-factor model) matched the two factor model proposed by Duro et al. (2010). Finally, we included a third model (one-factor second-order model) which considers that all the first-order factors are contributing to a common underlying second-order factor that we named "Cognition". With this latter model we intend to explore the unidimensionality tendency of the MoCA, similarly to what was found in some studies with other cognitive screening tests, as MMSE (e.g., Jones & Gallo, 2000).

II) Model assessment

To determine the best model, the three models were tested using the CFA and the model fit statistics compared. The fit statistics for each model, in total sample (*n* = 830), are summarized in Table 12.

Table 12. Fit indices of the Confirmatory Factor Analysis models

Models	χ^2	***d.f.***	***p***	$\chi^2/d.f.$	***CFI***	***TLI***	***RMSEA***
Six-factor Model	708.877	448	<.001	1.582	.981	.978	.026
Two-factor Model	1045.867	463	<.001	2.259	.956	.953	.039
One-factor Model (second-order)	872.094	457	<.001	1.908	.969	.966	.033

Abbreviations: χ^2: Chi-square test statistic; *d.f.*: degrees of freedom; $\chi^2/d.f.$: relative Chi-square; *CFI*: Comparative Fit Index; *TLI*: Tucker-Lewis Index; *RMSEA*: Root Mean Square Error of Approximation.

We can observe that the different fit models indices reflect good fit of the three models. All three models had a relative Chi-square close 2, the CFI and the TLI were above .95, and a *RMSEA* was less than .05. However, the six-factor model theoretically proposed by the authors showed a general better fit to the observed data in all the indices considered. The improved fit of six-factor model was significantly higher than the two-factor model in this study sample ($\Delta\chi^2_{(15)}$ = 269.165, p < .001) and than the one-factor second-order model ($\Delta\chi^2_{(9)}$ = 128.703, p < .001). The standardized factor weights and the item's squared multiple correlations of the six-factor model are compiled in Table 13. General factor weights and fit indices are suggestive of the MoCA six-factor factorial related validity.

Following the approach of Fornell and Larcker (1981), the composite reliability indices were computed for each latent factor. We found a value of .74 for Executive Function; .84 for Language; .89 for Visuospatial Skills; .87 for Short-term Memory; .91 for Attention, Concentration and Working Memory; and .95 for Orientation, which is indicative of good convergent related validity for each factor.

Given the fit results for the six-factor model we also examined the convergent and discriminant validity of the six factors using a stringent procedure outlined by Fornell and Larcker (1981). Regarding convergent validity, we computed the averaged variance extracted (AVE) which denotes the proportion of variance in the items explained by the underlying factor. The respective results range from .46 to .75, which is suggestive of appropriated convergent validity, according the criterion AVE >.5 (Fornell & Larcker, 1981). The discriminant validity of the factors was measured by comparing the AVE of each factor with the square of correlation between the factors. According to Fornell and Larcker (1981), two factors showed discriminant validity when the AVE is greater than the square of correlation between the factors. Except for Executive Functions and Language, which share the variance of the Phonemic Fluency, we have found discriminant validity between the factors.

Table 13. Standardized regression weights and squared multiple correlations for Six-factor Model

Latent and Observed Variables	Standardized Regression Weights	R^2
Factor 1: Executive Functions		
TMT-B (adapted)	.89	.79
Phonemic Fluency	.21	.04
Abstraction 1	.66	.44
Abstraction 2	.75	.56
Factor 2: Language		
Lion	.71	.51
Rhinoceros	.67	.45
Camel	.84	.71
Sentence 1	.70	.49
Sentence 2	.60	.36
Phonemic Fluency	.55	.30
Factor 3: Visuospatial Skills		
Cube	.79	.63
Contour	.84	.70
Numbers	.83	.69
Hands	.82	.67
Factor 4: Short-term Memory		
Word 1	.72	.51
Word 2	.75	.56
Word 3	.83	.69
Word 4	.65	.42
Word 5	.83	.68
Factor 5: Attention, Concentration and Working Memory		
Digits Forward	.61	.37
Digits Backward	.53	.28
Sustained Attention	.94	.89
Subtraction 1	.73	.53
Subtraction 2	.69	.48
Subtraction 3	.78	.62
Subtraction 4	.79	.62
Subtraction 5	.80	.63
Factor 6: Temporal and Spatial Orientation		
Date	.91	.83
Month	.90	.82
Year	.98	.95
Day	.91	.83
Place	.80	.64
City	.65	.43

DISCUSSION

The overall aim of the present study was to evaluate the factorial structure of the MoCA and analyze its construct related validity in cognitively healthy subjects, as well as in the MCI and the AD patients. To date, there were no other research studies of the factorial structure of the MoCA in community samples, and only one analyzed the dimensions underlying the MoCA in a heterogeneous clinical sample with cognitive decline. Thus, this study contributes to overcome a significant gap in the evaluation of the construct related validity of this instrument.

To provide further evidence to MoCA's construct related validity, several models were tested using CFA: a six-factor model based on the conceptual model proposed by the authors of the MoCA (Nasreddine et al., 2005); a two-factor model proposed by Duro et al. (2010); and a one-factor second-order model with all the first-order factors contributing to a common second-order factor "Cognition". Although all models showed a good fit in our data, the six-factor model showed the better absolute and relative fit indices, proving to have a significantly better fit than the others factorial models evaluated. Thus, this study corroborates the six-dimensional structure of the MoCA proposed by the authors. This six-dimensional approach was confirmed, not only by the improved fit of the model, but also by the validity analysis of the test where we were able to observe stronger intercorrelations between each item and the cognitive domains and between each cognitive domain and the MoCA total score. However, we found a lower contribution of the Phonemic Fluency task for the assessment of the Executive Function domain, so it is advisable to caution its interpretation in this sense.

The item analysis reveals an overall psychometric adequacy of the items of the MoCA. However, some problems were identified regarding the items Contour, Place, and City, which showed a higher hit rate and consequently lower correlations with any cognitive domain and with the total

score. However, these items did not compromise the overall six-factor model fit, showing an appropriated factor weights in model. The MoCA has also shown good reliability, either through the Cronbach's α or through the composite reliability indices.

Regarding to the MoCA's diagnostic accuracy to discriminate MCI and AD patients from cognitively healthy adults, with an optimal cut-off point below 22 points for the MCI patients, the MoCA showed a good sensitivity (81%) and specificity (77%). Likewise, with an optimal cut-off point below 17 points for the AD patients, the MoCA showed an excellent sensitivity (88%) and specificity (98%).

Our results allowed to establish the factorial, convergent and discriminant validity of the six-dimensional structure of the MoCA, and then proving its construct related validity. These findings permitted the calculation of performance profiles based on the results of the six cognitive dimensions. The possibility of a more comprehensive analysis of the performance in a brief cognitive screening test is a valuable advantage, resulting in an important contribution to outline a more systematic and comprehensive neuropsychological evaluation. Although the six-factor model shows the best fit, our findings allow to additionally support a second-order factor model, which considers that all the first-order factors are contributing to a common underlying second-order factor: "Cognition". This reveals a second-order unidimensional tendency, and serves as a good indicator that the MoCA, as a whole, evaluates individuals' global cognition (a positive finding considering that the MoCA is a brief cognitive screening instrument). The authors (Nasreddine et al., 2005) *a priori* hypothesized dimensions are consistent with the best MoCA's factor structure of this study. Indeed, this study provides additional evidence for the MoCA multifactorial nature, supporting the idea that this screening test does not measure only a global cognitive ability (total score) but the sub-scores extracted reflect different constructs or specific aspects of cognitive functioning, offering an empirical rational for examining separate indexes scores in the context of a profile

analysis. So, the MoCA interpretation could also examine the relative strengths and weaknesses (or higher and lower scores) for further additional hypothesis testing.

The current study has some limitations regarding the clinical samples size which did not allow a more detailed analysis of the MoCA´s structure in these groups. Some future considerations should be taken into account when analyzing the present results, namely the need for more studies conducted in different cultural contexts other than the Portuguese, as well as for different diagnostic groups, in order to further confirm the proposed six-dimensional structure underlying the MoCA and extend the present findings. Furthermore, it will be interesting to analyze the invariance of factorial structure across different groups, like diagnostic groups, age groups, and educational groups.

In summary, the MoCA has proved to be an appropriate measure for brief cognitive screening taking into account different cognitive domains such as: short-term memory; executive functions; visuospatial abilities; language; attention, concentration, working memory; and temporal and spatial orientation. These constructs have demonstrated to be structurally related. The present findings establish the factorial, convergent and discriminant validity, providing good evidence of the construct related validity of the MoCA, and will enable clinicians and others researchers to use this test, including the total score and also mainly their six latent dimensions in order to achieve a better understanding of the individuals' cognitive profile.

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All authors of this study declare that there are no conflicts of interest.

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ESTUDO IV

Montreal Cognitive Assessment (MoCA): Validation study for Mild Cognitive Impairment and Alzheimer´s Disease

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Abstract

The *Montreal Cognitive Assessment* (MoCA) was recently proposed as a cognitive screening test for milder forms of cognitive impairment, having surpassed the well-known limitations of the *Mini-Mental State Examination* (MMSE). This study aims to validate the MoCA for screening Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) through an analysis of diagnostic accuracy and the proposal of cut-offs. Patients were classified in two clinical-groups according to standard criteria: MCI (*n* = 90) and AD (*n* = 90). The two control-groups (C_MCI: *n* = 90; C_AD: *n* = 90) consisted of cognitively healthy community dwellers selected in order to match patients in gender, age and education. The MoCA showed consistently superior psychometric properties than the MMSE, and higher diagnostic accuracy to discriminate MCI (AUC = .856; 95% CI = .796 - .904) and AD patients (AUC = .980; 95% CI = .947 - .995). At an optimal cut-off of below 22 for MCI and below 17 for AD, the MoCA achieved significantly superior values in comparison to the MMSE for sensitivity, specificity, PPV, NPV, and classification accuracy. Furthermore, the MoCA revealed higher sensitivity to cognitive decline in longitudinal monitoring. This study provides robust evidence that the MoCA is a better cognitive instrument than the widely used MMSE for the screening and monitoring of MCI and AD in clinical settings.

Keywords: MoCA; neuropsychological test; cognitive screening; Mild Cognitive Impairment; Alzheimer's Disease.

INTRODUCTION

Cognitive impairment and dementia are the major health issues among older people. The Alzheimer´s disease (AD) is the most common neurodegenerative disorder with a prevalence of 4.4% for those older than 65 years old, and represents at least 60% of all dementia cases (Lobo et al., 2000). The serious impact of the AD in health-care systems worldwide (Comas-Herrera et al., 2011; Langa et al., 2001) and the dramatic projections for the coming years (Ferri et al., 2005; Wimo, Winblad, Aguero-Torres, & von Strauss, 2004) stress the need for new effective strategies able to slow or stop the disease progression. It is now generally accepted that prodromal AD is the ideal time window for disease modifying therapies.

Mild Cognitive Impairment (MCI) is considered a transitional stage between normal cognitive aging and impaired cognition caused by several pathologies, most frequently AD. This state of continuum is characterized by a deterioration of the cognitive functioning greater than expected for the person's age and educational level, but does not cause significant functional disability and is insufficient to establish the diagnosis of dementia (Petersen et al., 1999; Petersen, 2000, 2004, 2007). Longitudinal studies show that these patients progress to overt dementia at a rate of 10-15% *per* year, compared with a rate of 1-2% in the control subjects (Petersen et al., 1999). This explains why MCI is now the focus of prediction studies and the target of clinical trials of new disease modifying therapies.

The early screening of cognitive impairment and its differentiation from age related decline is thus extremely important. A brief and sensitive cognitive screening tool is indispensable to deal with this grey boundary area of normality between normal ageing, MCI and mild dementia. The *Montreal Cognitive Assessment* (MoCA; Nasreddine et al., 2005) is a novel international brief cognitive screening instrument developed for the detection of MCI and mild AD that may be suitable for this purpose. Previous studies have shown that the MoCA is useful and accurate in identification of milder

forms of cognitive impairment, having revealed a high sensitivity in the detection of MCI and AD patients (Damian et al., 2011; Fujiwara et al., 2010; Lee et al., 2008; Luis, Keegan, & Mullan, 2009; Rahman & Gaafary, 2009; Smith, Gildeh, & Holmes, 2007; Wen et al., 2008; Zhao et al., 2011). One of the reasons for the good sensitivity of the test is that it allows a more comprehensive assessment of the major cognitive domains, comparatively to other screening tests. This is the case of executive function, short-term memory, language skills and visuospatial processing. Furthermore, it has been demonstrated that the MoCA´s total score is an accurate quantitative estimate of the global cognitive ability in mild and moderate stages (Koski, Xie, & Finch, 2009; Koski, Xie, & Konsztowicz, 2011). Thus, beyond the routine screening, the MoCA scores can be used in longitudinal studies as an indicator of the global cognitive decline during the progression of the disease (Freitas, Santana, & Simões, 2010).

The aim of the present study is to validate the MoCA (Nasreddine et al., 2005; Simões et al., 2008) for cognitive screening of MCI and AD patients. This was carried out through the analysis of its diagnostic accuracy as well as the establishment of the optimal cut-off points to detect MCI and AD patients. The data of a longitudinal study with MCI and AD patients has also been analyzed in order to establish the MoCA's sensitivity for cognitive decline in a short period of time.

METHODS

Design

In the current study three groups of participants were considered: (I) MCI group, (II) AD group and (III) Control group. Patients were recruited at the Dementia Clinic, Neurology Department of the Coimbra University Hospital (Coimbra University Hospital, Coimbra, Portugal). Control subjects were selected from the database of the MoCA's normative study for the

Portuguese population (Freitas, Simões, Alves, & Santana, 2011) in order to match patients in gender, age and educational level. Two subgroups of patients belonging to both clinical groups (MCI and AD) were assessed at a second time point for preliminary longitudinal analysis.

Participants

The total study sample is composed of 360 participants distributed between three subgroups: (I) the MCI group with 90 patients, (II) the AD group with 90 patients, and (III) the Control group with 180 cognitively healthy adults. The demographic data of the participants in each group are provided in Table 1.

In order to exclude other causes of cognitive decline apart from a degenerative process, all patients were examined by a neurologist (IS) and a standard investigation were always performed, including laboratory routine exams/analysis - Apolipoprotein E (APOE) genotyping and imaging studies - structural (CT and/or MRI) and functional (SPECT). PET and cerebrospinal fluid analysis were carried out more restrictively, although considered in younger patients. All patients underwent a comprehensive neuropsychological assessment battery comprised at least by the following instruments: *Mini-Mental State Examination* (MMSE; Folstein, Folstein, & McHugh, 1975; Guerreiro, 1998), Alzheimer´s Disease Assessment Scale (ADAS; Rosen, Mohs, & Davis, 1984; Guerreiro, Fonseca, Barreto, & Garcia, 2008), Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982; Garret et al., 2008), Irregular Word Reading Test (TeLPI; Alves, Simões, & Martins, 2009) for pre-morbid intelligence estimate, Subjective Memory Complaints scale (SMC; Schmand, Jonker, Hooijer, & Lindeboom, 1996; Ginó et al., 2008) and Geriatric Depression Scale (GDS-30; Yesavage et al., 1983; Barreto, Leuschner, Santos, & Sobral, 2008). The MoCA was never used for diagnostic purposes. The diagnosis was established by a multidisciplinary team consensus considering the results of the comprehensive assessment and based on international criteria for MCI

of the Petersen workgroup (Petersen, 2004) and probable AD (APA, 2000; McKhann et al., 1984). The MCI group included patients classified as "amnestic MCI" (single or multidomain; Petersen, 2007) with a classification of 0.5 in the CDR. The AD group only included patients with mild to moderate severity (classified with CDR ≤ 2 and MMSE ≥ 12 points).

Control group participants were selected, as referred above, from the database of the MoCA's normative study for the Portuguese population (Freitas, et al., 2011). Each patient was matched to a cognitively healthy adult on variables shown to affect the MoCA´s performance (educational level and age; Freitas, et al., 2011) and additionally on gender, resulting in a perfect match between MCI and associated controls (then designated as the C-MCI group) and between AD and associated controls (C-AD group). Details regarding the controls' recruitment procedure, inclusion and exclusion criteria, and neuropsychological assessment have been described on the previous study (Freitas, et al., 2011).

Procedures

All participants were recruited between September 2008 and July 2010 and each participant was assessed in a single session by an expert in neuropsychology. Only patients with a stable clinical condition (without significant comorbidities), a complete clinical evaluation and already with a well-established diagnosis, according to the above international criteria, were considered to be eligible for this study. For each patient who was considered suitable for the study and at the time of the data collection, a diagnosis was recorded by the neurologist in the clinical file. These restrictive criteria imposed the exclusion of 30 patients that were still waiting for data considered essential in the differential diagnosis between AD and other dementias, and of those whose classification between MCI and AD was not fully established by the multidisciplinary team. Also at the outset of this study the exclusion criteria taken into account in the patients' selection were: higher dementia severity (CDR > 2 and MMSE < 12 points), recent

psychiatric comorbidities or therapeutic changes (6 months prior to the current neuropsychological evaluation), and significant motor, visual or auditory deficits, all of which may influence the neuropsychological assessment results.

For the preliminary analysis of the MoCA´s sensitivity to global cognitive decline in longitudinal monitoring we assessed two subgroups of patients (35 with MCI and 40 with AD) at a second time point, on average 176.81 ± 67.09 days apart (min.= 63; max.= 340).

The present research complied with the ethical guidelines for human experimentation stated in the Declaration of Helsinki and was approved by the Ethics Board of Coimbra University Hospital, by the "Fundação para a Ciência e Tecnologia" [Portuguese Foundation for Science and Technology] and by the Faculty of Psychology and Educational Sciences Scientific Committee. An informed consent was obtained from all the participants after the aims and research procedures were fully explained by a member of the study group. For the AD patients who were incapable of providing consent on his/her behalf, a legal representative provided it.

Neuropsychological testing and Materials

In the clinical interview the demographic and clinical data was collected through a complete sociodemographic questionnaire, an inventory of past habits and of the current clinical health status as well as of the medical history. Following this, the same neuropsychologist administered the MMSE (Folstein, et al., 1975; Guerreiro, 1998) and the MoCA (Nasreddine et al., 2005; Simões et al., 2008), in that fixed order for all the subjects. The MMSE is a widely recognized and used brief screening instrument for cognitive decline and therefore it is not described in detail here. Both the MMSE and the MoCA are in paper-and-pencil format and are scored out of a possible total score of 30 points, with higher scores indicating better cognitive performance. The MoCA was developed in order to screen milder forms of cognitive impairment, through the assessment of six cognitive

domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration and working memory; and temporal and spatial orientation (Nasreddine et al., 2005). It is composed by a one-page test, with an application time of approximately 10 to 15 minutes, and by a manual where explicit instructions concerning its administration and scoring system are available. The cultural adaptation process of the MoCA for the Portuguese population involved the translation, retroversion, linguistic improvement of the instrument and of the administration and scoring instruction manual, studies with the MoCA's Portuguese experimental version, the revision and adjustments required to finalize the MoCA's Portuguese final version, and an analysis of the equivalence between the original and the Portuguese final version, as described by Freitas and collaborators (2010). In the current study, the MoCA's total score refers to the raw score without correction point for education effects, considered in the original study (Nasreddine et al., 2005), since this correction is not used in the Portuguese population (Freitas, et al., 2011).

Statistical analysis

Statistical analyses were performed using the *Statistical Package for the Social Sciences* (SPSS, version 19.0) (IBM SPSS, Chicago, IL). Descriptive statistics were used for sample's characterization, and the χ^2 test and the two-sample *t*-test allowed the group comparisons. The Cronbach´s alpha was considered as an index of internal consistency. To assess test-retest reliability, intraclass correlation coefficients between scores at baseline and at follow-ups three and eighteen months later for the control participants were calculated. The interrater reliability was calculated using the Pearson correlation coefficient between the scoring of two independent evaluators. The convergent validity was determined using Pearson correlations coefficients between the MoCA scores and MMSE scores. The group differences were examined using two-sample *t*-test and

analysis of covariance. The preliminary data of longitudinal study were analyzed using paired-sample *t*-test.

The diagnostic accuracy of the MoCA and the MMSE for the prediction of the clinical diagnosis of MCI and AD was assessed through the receiver operating characteristics (ROC) curve analysis implemented in *MedCalc* (version 11.6) (MedCalc Software, Mariakerke). In this analysis, the areas under the curve (AUC) can vary between 0.5 and 1, with larger AUC indicates better diagnostic accuracy. The ROC curves were compared according to AUC comparison method of Hanley and McNeil (1983). The optimal cut-off points for each screening instrument that yielded the highest Youden index were selected, with higher Youden index indicating maximization of the sensitivity and specificity. For the analysis of the predictive value of these tests we calculated, for the each cut-off point, the sensitivity (the probability for subjects with cognitive impairment to have a positive test), specificity (the probability for subjects without cognitive impairment to have a negative test), positive predictive value (PPV, the probability of disease in subjects who have a positive test), negative predictive value (NPV, probability of the classification "lack of disease" in subjects who have a negative test) and classification accuracy (probability of correct classification of subjects with or without cognitive impairment).

RESULTS

Sample Characterization

Characteristics of the study sample, and in more detail of all the subgroups, are provided in Table 14. For this description were considered the following variables: sample size, educational level, age, gender, MMSE score and MoCA score.

As mentioned above, the control participants were selected from the database of MoCA's normative study for the Portuguese population (Freitas, et al., 2011) in order to match in educational level, age and gender to

patients of clinical groups. No statistically significant differences were found on the educational level ($t_{(178)} = .049$, $p = .961$), age ($t_{(178)} = .833$, $p = .406$), and gender ($\chi^2_{(1)} = .000$, $p = 1.0$) between the MCI and the C-MCI groups. Likewise, the AD and the C-AD group did not differ on the educational level ($t_{(178)} = .018$, $p = .986$), age ($t_{(178)} = .955$, $p = .341$) and gender ($\chi^2_{(1)} = .000$, $p = 1.0$). The MCI group and the AD group did not differ on the educational level ($t_{(178)} = .411$, $p = .681$) and gender ($\chi^2_{(1)} = .092$, $p = .761$), but nevertheless the AD patients were significantly older than MCI patients ($t_{(178)} = 3.071$, $p = .002$), due the average onset of symptoms in MCI precedes the onset of AD.

Table 14. Descriptive statistics for the sample's subgroups

Groups	*n*	Education	Age	Gender	MMSE	MoCA
MCI	90	6.50 ± 4.57	70.52 ± 7.95	55 (61.1)	27.08 ± 2.40	18.31 ± 3.87
C-MCI	90	6.53 ± 4.50	69.59 ± 7.05	55 (61.1)	28.88 ± 1.30	23.64 ± 3.22
AD	90	6.23 ± 4.12	74.22 ± 8.21	52 (57.8)	20.88 ± 4.09	10.06 ± 4.41
C-AD	90	6.24 ± 4.13	73.10 ± 7.54	52 (57.8)	28.09 ± 1.58	22.33 ± 3.47
Clinical	180	6.37 ± 4.34	72.37 ± 8.27	107 (59.4)	23.98 ± 4.57	14.18 ± 5.85
Control	180	6.39 ± 4.31	71.34 ± 7.49	107 (59.4)	28.48 ± 1.49	22.99 ± 3.40
Total	360	6.38 ± 4.32	71.86 ± 7.90	214 (59.4)	26.23 ± 4.07	18.59 ± 6.50

Abbreviations: MCI: Mild Cognitive Impairment patients; C-MCI: subgroup of controls matched with MCI patients; AD: Alzheimer's Disease patients; C-AD: subgroup of controls matched with AD patients; Clinical Group: all patients with MCI and AD; Control Group: all controls; MoCA: Montreal Cognitive Assessment (maximum score = 30); MMSE: Mini Mental State Examination (maximum score = 30);

Note: Gender is characterized by female's *n* and respective percentage (%). Data of others variables are presented as mean ± standard deviation.

Psychometric properties

The Cronbach´s alpha of the MoCA as an index of internal consistency was 0.903 for the total study sample, and the respective value for the MMSE was .856. Regarding the analysis of which MoCA items could be eliminated to increase the consistency, the results indicate that none should be excluded. The Cronbach´s alpha values in subgroups are provided in Table 15.

Table 15. Psychometric Properties

	Internal Consistency		**Reliability**			**Convergent Validity**
	Cronbach's α		Test-Retest		Interrater	Correlations MoCA / MMSE
	MoCA	MMSE	MoCA	MMSE		
MCI (*n* = 90)	.723	.617	3 months: .909 18 months: .877	3 months: .755 18 months: .665	.988	.601
AD (*n* = 90)	.824	.771				.700
C-MCI (*n* = 90)	.648	.457				.637
C-AD (*n* = 90)	.677	.402				.600
Total (n = 360)	.903	.856				.849

Abbreviations: MCI: Mild Cognitive Impairment patients; C-MCI: subgroup of controls matched with MCI patients; AD: Alzheimer's Disease patients; C-AD: subgroup of controls matched with AD patients; MoCA: Montreal Cognitive Assessment (maximum score = 30); MMSE: Mini Mental State Examination (maximum score = 30);

Note: Correlations values at a significant level $p < .01$

The test-retest reliability was measured through the intraclass correlation coefficient between the baseline and the follow-up data. This analysis was done only for the sub-sample of the control group in two follow-up settings: 3 months (*n* = 30; on average 146.87 ± 42.937 days apart; min.

= 68 days and max. = 200 days) and 18 months (n = 30; on average 515.04 ± 154.195 days apart; min. = 101 days and max. = 676 days). The obtained MoCA's values were respectively .909 and .877 and the correspondent values for the MMSE were respectively .755 and .665 (Table 2). The interrater reliability data was collected from a sub-sample of 60 tested participants of all groups and the obtained intraclass correlation index for the MoCA was .988. Another observation was that MoCA scores were highly and positively associated with MMSE scores (total study sample: r = .849, p < .001), which is indicative of convergent validity. The correlation's values in subgroups are presented in Table 15.

Group Differences

When analyzing the total sample, the MoCA scores were lower in AD group than in all other groups, and lower in MCI group than in both control groups, which do not differ between them ($t_{(178)}$ = 2.626, p = .225) (Table 14). Furthermore, we can observe that there were statistically significant differences when MoCA scores were compared between MCI and C-MCI groups ($t_{(178)}$ = 10.050, p < .001, mean difference = 5.333 ± .531) and between AD and C-AD groups ($t_{(178)}$ = 20.756, p < .001, mean difference = 12.278 ± .592). Since AD patients were significantly older than MCI patients, the analysis of differences in scores between clinical groups was performed using an analysis of covariance in order to control for the effects of age. It can be observed that the differences between MCI and AD patients scores ($F_{(1,177)}$ = 160.052, p < .001, η^2 = .48, mean difference = 7.930 ± .627) were in fact significant. The corresponding values for the MMSE were: I) MCI and C-MCI group: $t_{(178)}$ = 6.270, p < .001, mean difference = 1.800 ± .287; II) AD and C-AD group: $t_{(178)}$ = 15.603, p < .001, mean difference = 7.211 ± .462; and III) MCI and AD group: $F_{(1,177)}$ = 146.899, p < .001, η^2 = .45, mean difference = 6.231 ± .514. These results indicate that although the differences in the MMSE scores are statistically significant, the score differences obtained with the MoCA are more pronounced. A more detailed

analysis reveals that there were statistically significant differences in all cognitive domains of the MoCA in the three comparisons: I) MCI and C-MCI groups; II) AD and C-AD groups; and III) MCI and AD groups. Table 16 summarizes the results.

Table 16. Group differences in cognitive domains of the MoCA

Cognitive Domains	MCI and C-MCI	AD and C-AD	MCI and AD
Executive Functions	$t_{(178)} = 4.975$, $p < .001$	$t_{(178)} = 9.766$, $p < .001$	$t_{(178)} = 7.073$, $p < .001$
Visuospatial Skills	$t_{(178)} = 5.564$, $p < .001$	$t_{(178)} = 9.616$, $p < .001$	$t_{(178)} = 7.006$, $p < .001$
Short-term Memory	$t_{(178)} = 9.773$, $p < .001$	$t_{(178)} = 20.732$, $p < .001$	$t_{(178)} = 6.581$, $p < .001$
Language	$t_{(178)} = 2.964$, $p = .003$	$t_{(178)} = 8.800$, $p < .001$	$t_{(178)} = 7.010$, $p < .001$
Attention, Concentration and Working Memory	$t_{(178)} = 5.199$, $p < .001$	$t_{(178)} = 11.123$, $p < .001$	$t_{(178)} = 7.217$, $p < .001$
Temporal and Spatial Orientation	$t_{(178)} = 2.974$, $p = .003$	$t_{(178)} = 13.886$, $p < .001$	$t_{(178)} = 12.038$, $p < .001$

Abbreviations: MCI: MCI: Mild Cognitive Impairment patients; C-MCI: subgroup of controls matched with MCI patients; AD: Alzheimer's Disease patients; C-AD: subgroup of controls matched with AD patients.

Cut-off points

The receiver operating characteristics (ROC) curve analysis and the predictive values were performed to evaluate the diagnostic accuracy of MoCA to discriminate MCI and AD patients from cognitively healthy adult. Graphic representations of the ROC curves are provided in Figure 2.

It can be observed that both ROC curves referred to the MoCA fully include the curve for the MMSE, which is a clear indication that there is always a cut-off for the MoCA with higher sensitivity and specificity, for any

cut-off chosen for the MMSE. The discriminant potential of the MoCA for MCI was high, with an AUC of .856 (95% CI = .796-.904) and for AD was excellent, with an AUC of .980 (95% CI = .947-.995). In contrast, corresponding values for MMSE were .745 (95% CI = .674-.807) and .957 (95% CI = .916-.981). The AUCs for MCI are significantly different (z = 3.372, p = .0007), according to AUC comparison method of Hanley and McNeil (1983), indicating different classificatory accuracy of the instruments to milder cognitive impairment. No statistically significant differences were found between the AUCs for AD (z = 1.636, p = .1018). The optimal cut-off point for maximum accuracy (Youden index) and the respective values of sensitivity, specificity, PPV, NPV, and classification accuracy are described in Table 17.

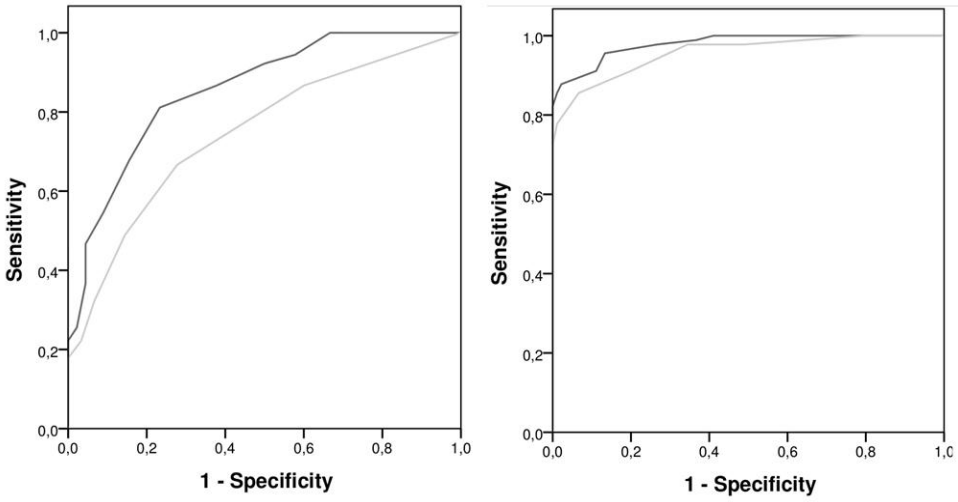

Figure 2. ROC curve analysis of the MoCA (dark gray) and MMSE (medium gray) to detect MCI (left) and AD (right).

Abbreviations: MoCA: Montreal Cognitive Assessment; MMSE: Mini Mental State Examination; MCI: Mild Cognitive Impairment; AD: Alzheimer's Disease.

Table 17. Diagnostic accuracy of the MoCA and MMSE to MCI and AD

	Cut-off	AUC	Sensitivity	Specificity	PPV	NPV	Classification Accuracy
MCI							
MoCA	< 22	.856	81	77	78	80	80
MMSE	< 29	.745	67	72	71	48	69
AD							
MoCA	< 17	.980	88	98	98	89	93
MMSE	< 26	.957	85	93	93	87	89

Abbreviations: MCI: Mild Cognitive Impairment patients; AD: Alzheimer's Disease patients; MoCA: Montreal Cognitive Assessment (maximum score = 30); MMSE: Mini Mental State Examination (maximum score = 30); AUC: area under the operating characteristic curve; PPV: positive predictive value; NPV: negative predictive value.

Note 1: Sensitivity, Specificity, PPV, NPV, and Classification Accuracy values were expressed in percentage.

Note 2: Cut-off values indicate the minimum score required for absence of signal.

The cut-off point of below 22 yielded the greatest Youden index for the MoCA in discrimination between MCI and controls. With this cut-off point, MoCA had a good sensitivity (81%), specificity (77%), PPV (78%), NPV (80%), classification accuracy (80%), and all these values were significantly superior comparing to the respective values for the MMSE. Furthermore, in what respects to the capacity of discrimination between AD patients and controls, once again the MoCA demonstrated an excellent sensitivity (88%), specificity (98%), PPV (98%), NPV (89%), and classification accuracy (93%) at the optimal cut-off of below 17 points, and again all these values were more favorable than the respective values for the MMSE.

Preliminary analysis of longitudinal study

For the preliminary analysis of the MoCA´s sensitivity to global cognitive decline during longitudinal monitoring, two clinical subgroups of

patients (35 with MCI and 40 with AD) were assessed at a second time point, on average 176.81 ± 67.09 days apart (min.= 63; max.= 340). When considering all patients (n = 75) statistically significant differences on MoCA scores were observed between both assessments ($t_{(74)}$ = 4.278, p < .001), in opposition to what was found with the MMSE ($t_{(74)}$ = 1.871, p = 065). A similar analysis for each clinical subgroup showed statistically significant differences on MoCA scores for both MCI ($t_{(34)}$ = 2.612, p = .014) and AD patients ($t_{(39)}$ = .5651, p < .001). An equivalent analysis using the MMSE revealed that the differences were significant for AD group ($t_{(39)}$ = 2.824, p = .008), while for MCI the MMSE showed no sensitivity to cognitive decline ($t_{(34)}$ = 1.873, p = .070). A more detailed and parceled analysis concerning the cognitive domains of the MoCA also revealed interesting results. When considering the total sample, the differences between the two evaluations were significant for visuospatial skills ($t_{(74)}$ = 2.487, p = .015); short-term memory ($t_{(74)}$ = 2.669, p = .009); attention, concentration and working memory ($t_{(74)}$ = 2.213, p = .030); temporal and spatial orientation ($t_{(74)}$ = 4.449, p < .001), and without significance for language and executive functions. When considering the clinical sub-groups, an isolated significant difference was founded for MCI patients in short-term memory domain ($t_{(34)}$ = 2.390, p = .023), while the same analysis for AD sub-group revealed statistical significance for attention, concentration and working memory ($t_{(39)}$ = 2.071, p = .045), and also for orientation ($t_{(39)}$ = 5.244, p < .001).

DISCUSSION

The main objective of this study was to validate the MoCA as a cognitive screening tool for MCI and AD. The results confirm its great potential and provide robust evidence that the MoCA is a better instrument for this purpose in comparison with the widely used MMSE. In fact, it was verified that the correlation coefficient between the two cognitive screening instruments was moderate to good, suggesting convergent validity. Nonetheless, the psychometric properties of the MoCA examined both in the

total sample and in each sub-groups, showed good properties and revealed to be consistently superior to those of the MMSE. As was previously referred, we believe that the two main reasons for the higher results of the MoCA at this level were: first, the inclusion of the executive functions assessment; and second, the consideration of more complex tasks to measure short-term memory, language, attention, concentration, working memory, and visuospatial skills.

Moreover, the analysis of group differences indicates that both instruments are able to distinguish the clinical and control groups. However, the differences between the groups were much more pronounced when the MoCA was used, in comparison with the MMSE, which is reflected in the consistently higher MoCA's mean differences. Furthermore, we observed statistically significant differences in all cognitive domains of the MoCA and in all group comparisons. These results confirm the higher capacity of the MoCA to discriminate between normal aging and pathological cognitive decline as well as between MCI and dementia.

The ROC curve analysis of the MoCA comparatively to the MMSE also showed that the MoCA exhibits a better diagnostic accuracy to discriminate MCI and AD patients from cognitively healthy adults. In our sample, the ideal cut-off point reached was lower than the original cut-off of 26 proposed by the authors (Nasreddine et al., 2005), as in other published results (Damian et al., 2011; Lee et al., 2008; Luis, et al., 2009; Zhao et al., 2011). We observed that at an optimal cut-off point below 22 for MCI, the MoCA had values significantly superior to the MMSE for sensitivity (81%), specificity (77%), PPV (78%), NPV (80%), and classification accuracy (80%). With an optimal cut-off of below 17 points for AD, the MoCA showed once again better results than the MMSE on sensitivity (88%), specificity (98%), PPV (98%), NPV (89%), and classification accuracy (93%). These results confirm that the MoCA is a better cognitive screening instrument for the detection of MCI and AD conditions comparatively to the MMSE, showing overall superior discrimination validity. The capacity of the MoCA to identify

different severity levels of cognitive decline justifies the pertinence of considering different cut-off points for MCI and dementia. This approach seems to be more useful and informative than a single cutoff point for cognitive decline as suggested in other studies, particularly in the original work of the Nasreddine and collaborators (2005).

An additional observation based on the present study regards the extremely poor diagnostic accuracy of the MMSE to identify MCI, reflected in overall low results, and mainly in poor sensitivity (67%), classification accuracy (69%), and very poor NPV (48%). This is a clear indication that whenever the MMSE is used to screen for milder forms of cognitive decline, the probability of false negatives cases is very high. This is especially critical under the current emphasis placed upon the early detection of cognitive impairment. Nonetheless, the MMSE remains the most commonly used screening tool despite the widely referred limitations in literature. Our results are a clear argument in favor of these opinions.

Finally, considering our analysis of the sensitivity of the MoCA to cognitive decline in patients that were longitudinally monitored, we could demonstrate evidences of decline in a short period of time. Furthermore, beyond its capacity to quantify cognitive decline, the MoCA also provides comprehensive information on the differential profile of clinical deterioration in MCI and AD.

We believe that the added value of the present study is the rigorous methodology used. It included: I) well-validated study samples (patients with misclassification and more advanced dementia cases were excluded, both characteristics susceptible of compromising the analysis of the discriminant capacity of the instruments); II) homogeneity of the clinical groups; III) a control sample with subjects recruited from the community and well-characterized as cognitively healthy adults; IV) equivalent samples sizes (which reduces the possible biases of sample sizes in statistical analysis); V) perfect matching between groups regarding sociodemographic characteristics that have a significant influence on the MoCA's performance;

and VI) rigorous MoCA' application, with no inter-rater variability (all participants were assessed by the same experienced neuropsychologist).

However, some limitations of the current study must be addressed. First of all, since only the amnestic subtype of MCI (single or multidomain) was considered, the generalization of the results to other forms of MCI should be cautious. Similarly, although the MoCA's Portuguese final version resulted of a rigorous process that followed the methodological guidelines for cultural adaptation studies, and the maximum equivalence between the original instrument and the MoCA's Portuguese final version was pursued (Freitas et al., 2010), the generalization of these results to other target populations should be cautious. On the other hand, the present study compares people with a clear diagnosis of AD/MCI with healthy people who not present health and cognitive difficulties, like the majority of the clinical validation studies of screening instruments. However, in the context of clinical applicability of a cognitive screening instrument, such as the MoCA, the most common diagnostic challenge is to identify clinical conditions among people with complaints of memory impairment or other cognitive difficulties or psychological disorders. Hence, we consider that such a question represents a very interesting challenge with a clear practical utility that should as such be a part of future efforts within this field of research. Finally, despite promising, the results of the preliminary analysis of the longitudinal evaluation require the corroboration by an ongoing study with longer follow ups and more robust samples.

In conclusion, this study produced several evidences of the overall superiority of the MoCA in comparison with the MMSE as a global cognitive assessment instrument, regarding the discriminant validity and the diagnostic accuracy. This was confirmed by the identification of MCI and AD and by the discrimination between both forms of cognitive decline and normal cognitive aging. Furthermore, the results suggest that the MoCA is sensitive to cognitive decline in a short period of time and may capture profiles of cognitive deterioration along the evolution of the disease. Thus,

this study shows a clear advantage in the use of the MoCA comparatively to the use of the MMSE, and brings together arguments for the use of the MoCA as a reliable brief cognitive instrument, which should be recommended both for screening and follow-up in primary clinical setting and geriatric health care.

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All authors of this study declare that there are no conflicts of interest.

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ESTUDO V

Montreal Cognitive Assessment (MoCA): Validition study for Frontotemporal Dementia

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Abstract

The *Montreal Cognitive Assessment* (MoCA) is a brief instrument developed for the screening of milder forms of cognitive impairment, having surpassed the well-known limitations of the MMSE. The aim of the present study was to validate the MoCA as a cognitive screening test for Frontotemporal dementia - behavioral variant (bv-FTD) by examining its psychometric properties and diagnostic accuracy. Three matched subgroups of participants were considered: bv-FTD (*n* = 50), AD (*n* = 50), and a control group of healthy adults (*n* = 50). Compared with the MMSE, the MoCA demonstrated consistently superior psychometric properties and discriminant capacity, providing comprehensive information about the patients' cognitive profiles. The MoCA's diagnostic accuracy for bv-FTD was extremely high [AUC (MoCA) = .934, 95%CI = .866-.974; AUC (MMSE) = .772, 95%CI = .677-.850]. With a cut-off below 17 points, the MoCA results for sensitivity, specificity, PPV, NPV, and classification accuracy were significantly superior to those of the MMSE. The MoCA is a sensitive and accurate instrument for the screening of bv-FTD patients and represents a better option than the MMSE.

Keywords: geriatric assessment; neuropsychological test; validation studies; cognitive impairment; Frontotemporal Dementia; Alzheimer disease.

INTRODUCTION

The diagnosis of Frontotemporal dementia remains a challenge wrapped in a nosologic controversy. Since the turn of the century, this clinical condition has been recognized and referred to as Pick's disease, Frontal lobe degeneration of non-Alzheimer's type, and Dementia of the frontal type, among other terms (Hutchinson & Mathias, 2007; Kertesz, Blair, McMonagle, & Munoz, 2008). The task force and consensus for new diagnostic criteria have proposed the designation of "Frontotemporal lobar degeneration" (Neary et al., 1998); however, the most frequently used term that currently gathers larger consensus is Frontotemporal dementia (FTD).

FTD refers to a group of degenerative dementias that are characterized by progressive, bilateral and more or less symmetrical pathology in the frontal and anterior temporal cortex (Seelaar, Rohrer, Pijnenburg, Fox, & van Swieten, 2011; Snowden, Neary, & Mann, 2002; Weder, Aziz, Wilkins, & Tampi, 2007). With an average onset age of approximately 50-60 years (Seelaar et al., 2008), FTD is the second most prevalent early-onset cause of degenerative dementia, after Alzheimer´s disease (AD). The few epidemiological studies available indicate a wide range of prevalence rates, with estimates of 15-22 per 100 000 people aged 45-64 years, which is almost half of the prevalence of AD in the same age cohort. The studies also estimate a prevalence rate of 9.4 per 100 000 for ages 60-69 years and a prevalence of 3.1 per 100 people aged 85 years or more (Seelaar et al., 2011; Weder et al., 2007). Overall, the estimates suggest that FTD is responsible for up to 20% of presenile dementia cases (Snowden et al., 2002; Weder et al., 2007). The genetic and chromosomal locus related to tau and progranulin proteins (Baker et al., 2006; Cruts et al., 2006; Hutton et al., 1998), as well as different neuropathological substrates that are now the basis for a pathological classification of FTD (Mackenzie et al., 2010; Seelaar et al., 2011), were initially described in this group of young familial cases.

Although FTD is a heterogeneous entity that produces a gradual but variable decline in behavioral, cognitive, and neurological domains (Neary et al., 1998; Seelaar et al., 2011; Weder et al., 2007), it has been widely accepted the division into three main subgroups, all of which contain corresponding topographical cerebral involvement:

Frontal-variant or *Behavioral-variant* is frequently referred to as *Frontotemporal Dementia* (bv-FTD) and is the most common subtype. bv-FTD accounts for approximately half of all FTD cases (Johnson et al., 2005; Seelaar et al., 2008). It is associated with bilateral, and usually symmetrical, frontal and anterior temporal dysfunction (Neary et al., 1998; Seelaar et al., 2011). Despite the heterogeneity in its clinical presentation, bv-FTD is characterized by an insidious onset and a progressive decline that is marked by personality and behavioral changes. These changes lead to an early decline in social interpersonal conduct, early impairment of regulation of personal conduct, and early emotional blunting and loss of insight (McKhann et al., 2001; Neary et al., 1998). The cognitive deficits that are most characteristic of bv-FTD are the impairment of executive function, attention and working memory deficits, poor abstraction, and difficulty shifting mental set with perseverative tendencies, all of which occur without severe amnesia, aphasia or perceptual dysfunction (Neary et al., 1998; Weder et al., 2007).

Semantic dementia (Snowden et al., 1989; Hodges et al., 1992) is also referred to *Semantic aphasia and associative agnosia* (Neary et al., 1998) or *Semantic variant of primary progressive aphasia* (Gorno-Tempini et al., 2011). It is usually correlated with left or bilateral atrophy of the middle and inferior temporal neocortex (Neary, Snowden, & Mann, 2005). The core feature of this clinical syndrome is a language disturbance that is characterized by fluent, effortless, and empty spontaneous speech, with severe deficits in naming and word comprehension and a loss of word meaning for both verbal and nonverbal concepts; another core feature is a perceptual disorder that includes prosopagnosia and associative agnosia

(Neary et al., 1998; Weder et al., 2007). For semantic dementia patients, some of the following abilities remain relatively preserved: repetition, articulatory abilities, ability to read aloud and to write down orthographically regular words that have been dictated, visuospatial skills, working memory and autobiographical memory, at least for the recent past (Neary et al., 1998; Weder et al., 2007).

Progressive nonfluent aphasia (Neary et al., 1998), also called *Nonfluent/agrammatic variant of primary progressive aphasia* (Gorno-Tempini et al., 2011), is associated with asymmetric atrophy of the left hemisphere (Neary et al., 2005). This is a disorder of expressive language that usually occurs without impairments in other cognitive domains. These patients present nonfluent spontaneous speech that is marked by agrammatism, phonemic paraphasias and anomia, with difficulties in reading and writing. Word comprehension remains relatively well preserved and behavioral symptoms are less common among these patients than among sufferers of the other two types of FTD (Neary et al., 1998).

Several studies have examined the neuropsychological deficits in FTD patients (Diehl et al., 2005; Gregory, Orrell, Sahakian, & Hodges, 1997; Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000; Perry & Hodges, 2000; Thompson, Stopford, Snowden, & Neary, 2005). These studies were designed to identify a global characterization of FTD, which would be a valuable contribution to distinguishing FTD from other dementia diagnoses. However, the clinical heterogeneity of FTD, its decline in domains beyond the cognitive, which are not evaluated by neuropsychological tests, the overlap of some cognitive deficits between FTD and other types of dementia as well as the methodological differences across study designs have contributed to inconsistent findings and difficulties in the early distinction between FTD and others dementias using neuropsychological tools (Hutchinson & Mathias, 2007; Seelaar et al., 2011; Thompson et al., 2005). This lack of distinction is particularly relevant for AD, with which there appears to exist greater misdiagnosis. Moreover, numerical scores on

cognitive tests have a limited value in differentiating between FTD and AD, while qualitative performances and error types appear to enhance this distinction (Gregory et al., 1997; Hutchinson & Mathias, 2007; Mathuranath et al., 2000; Perry & Hodges, 2000; Thompson et al., 2005).

The significant increase in prevalence rates, the recent advances in genetic diagnosis and familial counseling, and different orientations in terms of pharmacological treatment all highlight the importance of an accurate screening during early stages of these disorders. The Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) is the most widely used and validated screening instrument for the assessment of cognitive function. However, several limitations have been identified in the literature, namely, the low sensitivity to the early stages of AD and the inability to differentiate between the various dementia disorders (Freitas, Santana, & Simões, 2010; Ihl, Frölich, Martin, & Maurer, 1992; Mathuranath et al., 2000; Tombaugh & McIntyre, 1992; Wind et al., 1997). Regarding FTD, several studies have reported that the MMSE lacks enough sensitivity to identify cognitive impairments and frequently results in normal test performance, which is especially problematic in cases of isolated frontal or linguistic deficits that are typical of the early stages (Gregory & Hodges, 1996; Gregory et al., 1997; Hodges et al., 1999; Miller et al., 1991; Weder et al., 2007). This lack of sensitivity results from the low complexity of the tasks for assessment of memory and language dysfunctions and from the lack of tasks for the evaluation of executive function (Mathuranath et al., 2000; Naugle & Kawczak, 1989).

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a recent international brief cognitive screening instrument that was developed to detect milder forms of cognitive impairment, overcoming limitations of the MMSE. Previous studies have reported the usefulness of MoCA in accurately identifying milder forms of cognitive impairment. Compared with the MMSE, the MoCA displays a higher sensitivity in detecting MCI and AD patients (Freitas, Simões, Alves, & Santana, 2012;

Fujiwara et al., 2010; Lee et al., 2008; Luis, Keegan, & Mullan, 2009; Rahman & Gaafary, 2009; Smith, Gildeh, & Holmes, 2007; Zhao et al., 2011). This improved sensitivity explains the MoCA's widespread international use and its recognition as one of the best screening tests (Ismail, Rajji, & Shulman, 2009; Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Lonie, Tierney, & Ebmeier, 2009). One of the reasons for the good sensitivity of the test is that it allows a more comprehensive assessment of the major cognitive domains, comparatively to other screening tests, especially executive functions and short-term memory, but also of language abilities and visuospatial processing. Despite the recognition that the MoCA has received as a screening tool, its diagnostic sensitivity cannot be generalized to FTD because there are no published studies validating the MoCA for these patients.

The general aim of this study is to validate the MoCA as a cognitive screening test for bv-FTD by examining its psychometric properties and diagnostic accuracy. Furthermore, we also investigated the cognitive performances of bv-FTD patients on the MoCA and analyzed how their performances differed from AD patients.

METHOD

Participants and Procedures

The total sample includes 150 participants divided into three subgroups: I) a bv-FTD group with 50 patients, II) an AD group with 50 patients, and III) a Healthy group comprising 50 cognitively healthy adults.

Both clinical groups were recruited between January 2009 and June 2011 at the Dementia Clinic of the Neurology Department of Coimbra University Hospital (Coimbra, Portugal). Study eligibility was restricted to patients with a comprehensive clinical/neuropsychological evaluation and a full investigation using biochemical, structural and functional imaging (MRI

and SPECT and/or PET), which are essential to exclude other causes of no degenerative dementia.

The bv-FTD group included only those patients who displayed the behavioral variant of FTD diagnosis, as established by a multidisciplinary team according to international criteria (Neary et al., 1998). All of the individuals who displayed the aphasic syndromes of FTD or mixed clinical syndromes were excluded from the study. All of the bv-FTD patients underwent a comprehensive neuropsychological assessment battery, which was comprised of the following instruments: the Neuropsychiatric Inventory (NPI; Cummings et al., 1994), the Frontal Behavior Inventory (FBI; Kertesz, Nadkami, Davidson, & Thomas, 2000), the Comprehensive Affect Testing System (CATS; Schaffer, Froming, Gregory, Levy, & Ekman, 2006), the Frontal Assessment Battery (FAB; Dubois, Slachevsky, Litvan, & Pillon, 2000), the MMSE (Folstein et al., 1975), the Trail Making Test (TMT; Partington & Leiter, 1949), Verbal Fluency (Garcia, 1984), the Maze-Tracing Task (Lezak, Howieson, & Loring, 2004), the Digit Span Test (Wechsler, 2008), the Digit Symbol Test (Wechsler, 2008), the Spatial Span Test (Wechsler, 2008), the Token Test (De Renzi et al., 1962; Garcia, 1984), the Buschke Selective Reminding Test (Buschke, 1973), and the Brief Visuospatial Memory Test (Benedict, 1997).

The AD group included only those patients who were diagnosed by a multidisciplinary team consensus based on international criteria for probable AD (APA, 2000; McKhann et al., 1984). This group was recruited to match the bv-FTD patients by gender, age, education level, and severity of cognitive decline, as assessed by the MMSE. All of the AD patients were administered a comprehensive clinical evaluation and underwent the following comprehensive neuropsychological assessment battery: the MMSE (Folstein et al., 1975), the Alzheimer´s Disease Assessment Scale (ADAS; Rosen, Mohs, & Davis, 1984), the Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982), the Irregular Word Reading Test (TeLPI; Alves, Simões, & Martins, 2009) as an estimate of pre-

morbid intelligence, the Subjective Memory Complaints scale (SMC; Schmand, Jonker, Hooijer, & Lindeboom, 1996) and the Geriatric Depression Scale (GDS-30; Yesavage et al., 1983).

The following patient exclusion criteria were established at the outset of the study: an unstable clinical condition, with significant comorbidities; high severity dementia (only those patients with CDR ≤ 2 and MMSE ≥ 12 points were included in the study); recent pharmacotherapy changes; recent psychiatric comorbidity (clinically diagnosed within the 6 months prior to the current neuropsychological evaluation); and significant motor, visual or auditory deficits, all of which may influence neuropsychological assessment.

The healthy group comprised cognitively healthy community members who resided in the Portuguese continental territory. This group was selected from the database of MoCA's normative study for the Portuguese population in order to match each patient on variables that were found to be predictive of the MoCA´s performance (educational level and age; Freitas, et al., 2012), and additionally on gender. Details of the control participants' recruitment procedure, inclusion and exclusion criteria, and neuropsychological assessment have been described in a previous study (Freitas et al., 2011).

Informed consent was obtained from all of the participants after a member of the research team provided them with a full explanation of the research aims and procedures as well as confidentiality requirements. For the patients who were not capable of providing the informed consent, a legal representative fulfilled that requirement on their behalf. The present research complies with the ethical guidelines on human experimentation stated in the Declaration of Helsinki and was approved by the Portuguese Foundation for Science and Technology and by the Faculty of Psychology and Educational Sciences Scientific Committee.

Material and Neuropsychological testing

In the clinical interview, data were collected through a comprehensive sociodemographic questionnaire and an inventory of the patients' current clinical health status, past habits and medical history. The diagnosis of bv-FTD requires significant input from a close informant; thus, an extensive interview was conducted with each patient´s caregiver. The informants also contributed to the completion of some of the assessment tests listed above. For the purposes of this study, the neuropsychologist administered the MMSE (Folstein et al., 1975; Guerreiro et al., 1998) and the MoCA (Nasreddine et al., 2005; Simões et al., 2008) in a single session. All of subjects received the MMSE first.

The MMSE is the most widely recognized and used brief screening instrument for detecting cognitive deficits. Both the MMSE and the MoCA are brief cognitive screening tools that are administered in paper-and-pencil format. For both tests, a score is derived by summing the points from each successfully completed task, for a total range from 0 to 30 points; higher scores indicate better cognitive performance. The MoCA was developed to screen milder forms of cognitive impairment through the assessment of a wide range of cognitive functions, such as short-term memory, executive functions, visuospatial abilities, language, attention, concentration, working memory, and temporal and spatial orientation (Nasreddine et al., 2005). It comprises a one-page test, which requires a short administration time (10 to 15 minutes). The MoCA is accompanied by a manual that explicitly describes the instructions for administering the tasks and objectively defines the scoring system. In the current study, the MoCA's total score refers to the raw score without the one correction point for education effects that was recommended in the original study (Nasreddine et al., 2005) because this correction is not used in the Portuguese population (Freitas et al., 2011).

Statistical Analyses

Statistical analyses of the data were computed using the Statistical Package for the Social Sciences (SPSS, version 19.0) (IBM SPSS, Chicago, IL). Descriptive statistics were used for the sample's characterization. The χ^2 test, the two-sample *t*-test, the one-way between-groups analysis of variance (ANOVA), and the Tukey HSD and Bonferroni post-hoc test were conducted to examine group differences. Cronbach´s alpha was used as an index of internal consistency. The Pearson correlation coefficients were used to analyze inter-rater reliability and convergent validity and to explore the correlations between items, cognitive domains and the total test score.

The diagnostic accuracy of the MoCA and the MMSE for predicting clinically diagnosed bv-FTD was assessed through the receiver operating characteristics (ROC) curve analysis implemented in MedCalc (version 11.6) (MedCalc Software, Mariakerke). The area under the curve (AUC) was calculated, which can vary between 0.5 and 1, with a larger AUC signifying better diagnostic accuracy. The ROC curves were compared according to Hanley and McNeil's (1983) AUC comparison method. For each instrument, the optimal cut-off points that yielded the highest Youden index were selected, with a higher Youden index indicating the maximization of the instrument's sensibility and specificity. To analyze the predictive value of the tests, for each cut-off point, we calculated: the sensibility (the probability that subjects with cognitive impairment will test positive), specificity (the probability that subjects without cognitive impairment will test negative), positive predictive value (PPV; the probability of disease in subjects who test positive), negative predictive value (NPV; the probability of a lack of disease in subjects who test negative) and classification accuracy (the probability of correctly classifying subjects who either do or do not have cognitive impairment).

RESULTS

Sample Characterization

Table 18 presents the characteristics of the sample, including details for all of the subgroups. The following variables were included in the sample characterization: sample size, gender, age, educational level, time progression of the disease, family history, MMSE score, and MoCA score.

Table 18. Demographic and clinical characteristics of the subgroups.

	bv-FTD	**AD**	**Healthy**
n	50	50	50
Gender	25 (50.0)	25 (50.0)	25 (50.0)
Age	67.96 ± 7.69	70.64 ± 7.51	70.12 ± 7.22
Educational Level	6.18 ± 3.71	6.14 ± 3.88	6.26 ± 3.83
Time progression of disease	3.24 ± 2.80	3.94 ± 2.60	-
Family history	7 (14.0)	25 (50.0)	7 (14.0)
MMSE score	23.86 ± 4.76	22.46 ± 3.81	27.88 ± 1.71
MoCA score	13.34 ± 5.03	11.04 ± 4.46	22.50 ± 3.44

Abbreviations: bv-FTD = group of patients with behavioral variant of Frontotemporal dementia; AD = group of patients with Alzheimer´s disease; Healthy = group of cognitively healthy adults; MoCA = Montreal Cognitive Assessment (maximum score = 30); MMSE = Mini Mental State Examination (maximum score = 30).

Note: Gender is characterized by female's *n* and respective percentage (%). Time progression of disease is expressed in years. Family history is characterized by positive cases' *n* and respective percentage (%). Data of others variables are presented as mean ± standard deviation.

As presented in Table 18, there are no gender differences between the three groups. Similarly, no statistically significant differences were found between groups for age ($F_{(2,147)} = 1.808$, $p = .168$) or educational level (F

$_{(2,147)}$ = .013, p = .987). In addition, the clinical groups did not differ from each other in terms of MMSE score ($t_{(98)}$ = 1.622, p = .108), which suggests an equivalence across groups in the severity of cognitive decline. Regarding the time of progression disease no statistically significant differences were found between the clinical groups ($t_{(98)}$ = 1.295, p = .198). Finally, half of the AD group patients had a family history of dementia in first-degree relatives, whereas the bv-FTD group and the healthy group did not differ from each other; approximately 14% of each group presented positive cases in their family history.

Psychometric properties

Internal consistency reliability of the MoCA was estimated using Cronbach's α. In the total sample, we found a Cronbach's α of .906 that confirms the overall reliability of the scale when used to examine Portuguese subjects (the respective value for MMSE was .832). A more detailed analysis reveals that excluding any single item from the scale does not improve the reliability coefficient value. This reliability coefficient was also computed for each clinical group: α (bv-FTD) = .847; and α (AD) = .835. The inter-rater reliability was calculated for a sub-sample of 30 bv-FTD patients and resulted in a high Pearson correlation of .976. The correlations between the MoCA scores and the MMSE scores were also explored. A high positive correlation was observed between the scores from both tools in the total sample (r = .802, p < .001) and in the bv-FTD group (r = .838, p < .001), which is indicative of convergent validity. Both the correlations between each item and the cognitive domains, and between each cognitive domain and the overall MoCA score were also analyzed in the bv-FTD group. All of the items showed a significantly higher correlation with their respective domains than with any other domain. In this sample, the Phonemic Fluency task showed a higher correlation with the Executive Function domain than with Language domain. Furthermore, we found a significant (p <.001) positive correlation between each cognitive domain and the total score of the scale, ranging

from .349 to .787. These correlations are suggestive of construct related validity. Furthermore, each domain showed significantly higher correlations with the MoCA total score than with any other domain, illustrating the discriminative power of the domains.

Group Differences

There were statistically significant differences between the groups in the MoCA total scores ($F_{(2,147)} = 96.700$, $p < .001$). According to *post-hoc* tests, these differences occurred between all group comparisons. Thus, although the clinical groups were previously matched for the severity level of their cognitive decline, as assessed by the MMSE ($t_{(98)} = 1.622$, $p = .108$), the AD patients obtained significant lower MoCA scores (11.04 ± 4.46) than the bv-FTD patients (13.34 ± 5.03), and both clinical groups obtained lower scores than the healthy group (22.50 ± 3.44).

As expected, a more detailed analysis regarding the sub-scores from the MoCA cognitive domains revealed that the healthy participants performed higher in all cognitive domains than both clinical groups. Comparing the two clinical groups, statistically significant differences in both the short-term Memory domain and the Attention, Concentration and Working Memory domain were observed, with the AD patients performing worse than the bv-FTD patients, according to *post-hoc* tests [AD group: Memory domain (range 0 to 5) = .16 ± .510; Attention, Concentration and Working Memory domain (range 0 to 6) = 2.42 ± 1.655; bv-FTD group: Memory domain = .72 ± 1.230; Attention, Concentration and Working Memory domain = 3.30 ± 1.799].

Cut-off points

The receiver operating characteristics (ROC) curve analyses were computed to evaluate the diagnostic accuracy of the MoCA and the MMSE to discriminate the bv-FTD patients from the cognitively healthy adults. Graphic representations of the ROC curves are provided in Figure 3.

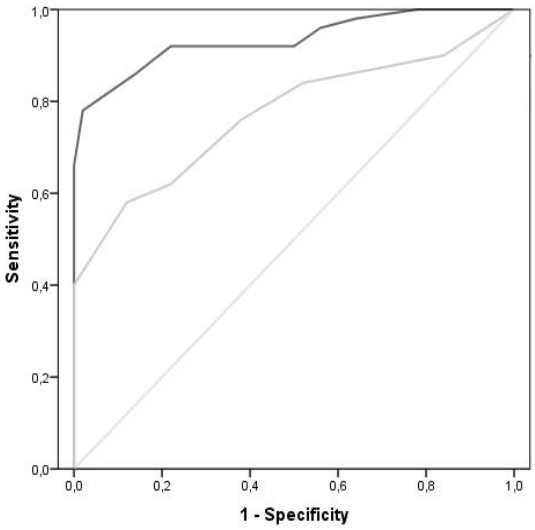

Figure 3. ROC curve analysis of the MoCA (dark gray) and MMSE (medium gray) to detect FTDbv, with reference line (light gray diagonal).

Abbreviations: MoCA: Montreal Cognitive Assessment; MMSE: Mini Mental State Examination; FTDbv: Frontotemporal dementia, behavioral variant.

The MoCA discriminant potential for bv-FTD was excellent, with an AUC of .934 (95% confidence interval = .866 - .974). In contrast, the MMSE showed an acceptable discriminant potential, with a corresponding AUC of .772 (95% confidence interval = .677 - .850). These AUC were significantly different from each other (z = 4.472, p < .001), according to the AUC comparison method of Hanley and McNeil (1983), indicating that the instruments were different in the accuracy of their classifications.

Figure 3 illustrates that the ROC curve for the MoCA fully included the curve for the MMSE, which is a clear indication that there is always a cut-off for the MoCA, with higher sensitivity and specificity, for any cut-off chosen for the MMSE. The optimal cut-off point for maximum accuracy

(Youden index) and the respective values of sensitivity, specificity, PPV, NPV, and classification accuracy are described for both instruments in Table 19.

Table 19. Diagnostic accuracy of the MoCA and MMSE to bv-FTD

	Cut-off	Sensitivity	Specificity	PPV	NPV	Classification Accuracy
MoCA	< 17	78	98	98	82	88
MMSE	< 26	58	88	83	68	73

Abbreviations: MoCA: Montreal Cognitive Assessment (maximum score = 30); MMSE: Mini Mental State Examination (maximum score = 30); AUC: area under the operating characteristic curve; PPV: positive predictive value; NPV: negative predictive value.

Note 1: Sensitivity, Specificity, PPV, NPV, and Classification Accuracy values were expressed in percentage.

Note 2: Cut-off values indicate the minimum score required for absence of signal.

DISCUSSION

This study was primarily motivated by the lack of studies validating the MoCA as a brief cognitive screening instrument for bv-FTD patients and by the need for a sensitive, reliable and accurate instrument to briefly assess the cognitive impairments in these patients. In this context, three matched subgroups of participants (bv-FTD, AD, and Healthy group) were investigated to validate the MoCA for bv-FTD patients, to establish the MoCA's corresponding cut-off point, and to evaluate its diagnostic classification accuracy. Our findings demonstrate the MoCA´s adequacy and usefulness for this task and indicate that the MoCA is superior to the widely used MMSE as a brief cognitive assessment of bv-FTD patients.

The MoCA consistently displayed superior psychometric properties than the MMSE, which confirm the overall reliability of the scale when used to examine Portuguese subjects. We consider that the presence of a manual

with administration and scoring rules for the tasks contributed to the MoCA's excellent interrater reliability. The correlation coefficient between the MoCA's and the MMSE's total scores was high, suggesting convergent validity. Finally, significant positive correlations were found between each item and its respective cognitive domain, and all of the items were more highly correlated with their own respective domain than with any other domain. Each cognitive domain was more highly correlated with the MoCA total score than with any other domain. These correlations support both the MoCA´s construct related validity and the discriminative power of the cognitive domains.

As expected, the healthy participants obtained higher MoCA scores than either of the clinical groups. Despite the previous matching according to the severity level, as assessed by the MMSE, we found statistically significant differences between the two clinical groups in the MoCA scores, with a lower performance displayed by the AD patients. This finding demonstrates that the MoCA has better discriminant capacity than the MMSE. At the level of the MoCA´s cognitive domains, the healthy participants also had significantly higher performances than both patients groups in all cognitive domains. Between clinical groups, statistically significant differences were observed in the MoCA's short-term memory and visuospatial domains, with the AD patients performing worse than the bv-FTD patients. However, these results should be interpreted cautiously because they contribute to a literature that already presents several inconsistencies. Various factors have contributed to the difficulties in distinguishing between FTD and other dementias at early stages of the disease using neuropsychological tools (Hutchinson & Mathias, 2007; Seelaar et al., 2011; Thompson et al., 2005), including the clinical heterogeneity of FTD, its decline in other domains beyond the cognitive, which are not evaluated by neuropsychological tests, the overlap in some cognitive deficits between FTD and other types of dementia, and the methodological differences across the study designs (variation in the mean

age of participants, diagnostic criteria, mixed clinical groups that include different FTD subtypes, and the stage of the disease's evolution).

The MoCA displayed excellent diagnostic accuracy in discriminating bv-FTD patients from cognitively healthy old adults, and it exhibited an AUC that was significantly higher than the MMSE's AUC. The optimal cut-off point for detecting bv-FTD that allowed the maximization of the sensibility and specificity was below 17 points. This cut-off point is equivalent to the optimal cut-off point established in our prior MoCA's validation studies for AD patients (Freitas et al., 2012) and for Vascular Dementia patients (Freitas, Simões, Alves, Vicente & Santana, *submitted*). With this cut-off point, the MoCA showed high levels of sensitivity (78%), specificity (98%), PPV (98%), NPV (82%), and classification accuracy (88%); all of the values were consistent and significantly higher than the respective MMSE values. In this sample, the MMSE's optimal cut-off point to detect bv-FTD was below 26 points.

We propose that the current study's strengths include the homogeneity of the sample regarding groups' size, gender, age, educational level and severity level of cognitive decline (as assessed by the MMSE in the clinical groups) as well as the homogeneity in the FTD group (for which only the behavioral variant was considered). These strengths allowed a clearer analysis and minimized the influence of these individual and methodological variables. Additionally, contributions to the current study's methodological rigor included the previous well-validated clinical diagnosis of groups by a multidisciplinary team using standard criteria and based on a full investigation, the presence of a control group composed of cognitively healthy adults from the community, and the reduced inter-rater variability due to evaluation of the participants by one of two expert neuropsychologists.

However, some limitations of current study must be addressed, mainly, that our analyses included only those FTD patients who displayed the behavioral variant. Caution should be used when generalizing these

results to other FTD syndromes, and homogeneous groups from the other FTD syndromes should be investigated in the future. The current study is the first to validate the MoCA for screening bv-FTD and to examine its diagnostic accuracy with the establishment of cut-off points; thus, we cannot compare it with other studies.

In conclusion, MoCA was confirmed as a valid, reliable, sensitive and accurate instrument for the brief assessment of cognitive impairments in bv-FTD patients. The MoCA results were systematically superior to the MMSE results for both discriminant validity and diagnostic accuracy. Therefore, MoCA is a better cognitive screening instrument for bv-FTD than the MMSE.

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ESTUDO VI

Montreal Cognitive Assessment (MoCA): Validition study for Vascular Dementia

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Abstract

The Montreal Cognitive Assessment (MoCA) is a brief instrument developed for the screening of milder forms of cognitive impairment, having surpassed the well-known limitations of the MMSE. The aim of the present study was to validate the MoCA as well as its short version, which was proposed by the NINDS-CSN VCI Harmonization Standards for screening Vascular Dementia (VaD) patients. The results, based on a homogeneity sample of 34 VaD patients, indicate that the MoCA is a psychometrically valid and reliable instrument for cognitive screening in VaD patients, showing excellent discriminant validity. Both the full and short versions of the MoCA had excellent diagnostic accuracy in discriminating VaD patients, exhibiting an AUC significantly higher than the MMSE [AUC (MoCA full version) = .950; 95% CI = .868 - .988; AUC (MoCA short version) = .936; 95% CI = .849 - .981; AUC (MMSE) = .860; 95% CI = .754 - .932]. With a cut-off below 17 on the MoCA full version and 8 on the short version, the results for sensitivity, specificity, positive and negative predictive values, and classification accuracy were significantly superior compared to the MMSE. In conclusion, both versions of the MoCA are valid, reliable, sensitive and accurate screening instruments for VaD patients.

Keywords: geriatric assessment; neuropsychological test; validation studies; cognition; Vascular Dementia; Alzheimer disease;

INTRODUCTION

Epidemiological studies, although not consistent, have generally reported that Vascular Dementia (VaD) is the second most common cause of dementia, after Alzheimer´s disease (AD) (Canadian Study of Health and Aging Working Group, 1994; Lobo et al., 2000). In Europe, the prevalence rate is approximately 16/1000 in people over 65 years old, representing approximately 20% of all dementia cases (Fratiglioni et al., 2000; Lobo et al., 2000). Moreover, in some Asian countries, VaD appears to be more prevalent than AD (Ikeda et al., 2001; Ueda, Kawano, Hasuo, & Fujishima, 1992). Both prevalence and incidence of VaD and AD increase exponentially with age, and even though the increase in VaD seems to be less steep than for AD, the prevalence rate for individuals over 100 years old surpasses 52/1000. (Jorm & O'Brien, 2004; Lobo et al., 2000).

In recent years, the nosologic concept of vascular cognitive impairment and dementia has generated a huge controversy and disagreement regarding diagnostic criteria. This was, in fact, one of the major causes of the discrepancy observed in epidemiological studies. The existence of many cases of cognitive deficit resulting from cerebrovascular disease but not fulfilling the criteria for dementia has led to the recent emergence of a broader concept named Vascular Cognitive Impairment (VCI; Hachinsky & Bowler 1993; O´Brien, Reisberg, & Erkinjuntti, 2003). The VCI represents a heterogeneous group of cognitive disorders, in terms of typology and degree of impairment, arising from different types of cerebrovascular disease. Three diagnostic categories are mainly proposed: Vascular Mild Cognitive Impairment (vMCI, also known as Vascular Impairment No Dementia, VCIND), Vascular Dementia (VaD), and mixed dementia (Moorhouse & Rockwood, 2008; O´Brien et al., 2003). The vMCI includes those individuals with cognitive impairment of presumed vascular etiology that do not display a substantial functional impairment. These patients do not meet criteria for dementia but have a high risk of progression

to dementia, particularly if they have recurrent stroke (Moorhouse & Rockwood, 2008; O´Brien et al., 2003). The VaD diagnosis was reserved for VCI cases that met operationalized criteria for dementia, including disorders considered in the original vascular dementia construct (e.g., poststroke dementia, multi-infarct dementia, subcortical ischemic vascular dementia, or small-vessel dementia) (Moorhouse & Rockwood, 2008; O´Brien et al., 2003). The mixed dementia classification included patients with concomitant clinical features of primary neurodegenerative dementia, mostly AD, and vascular lesions (Moorhouse & Rockwood, 2008). This coexistence is now well recognized, particularly in older people; it leads to an acceleration of the clinical expression of overt dementia, as well as to an increase in the severity of dementia among AD patients (Snowdon et al. 1997; Desmond, 2004; Román, 2003). Moreover, neuropathologic studies suggest that mixed dementia may be even more common than previously documented, constituting the most common form in the general population (Bowler, Munoz, Merskey, & Hachinski, 1998; Lim et al., 1999; Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study, 2001; O´Brien et al., 2003).

The concept of VaD, which is classified as a VCI subtype, was introduced in the 1990s (Román et al., 1993), replacing the previous concepts of Cerebral Arteriosclerosis and Multi-infarct dementia (Hachinki, Lassen, & Marshall, 1974). This concept´s evolution was associated with the proposal of new diagnostic criteria for Vascular Dementia by the National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN; Román et al., 1993). These criteria were organized and further operationalized by van Straaten and collaborators (2003), considering three fundamental axes of diagnosis: a) presence of dementia, confirmed by neuropsychological assessment; b) clinical and imaging evidence of cerebrovascular disease; and c) establishment of a causal relationship between the vascular lesions and the emergence or aggravation of the

cognitive deficits. The harmonization and coverage of clinical, neuroimaging, and anatomic-pathologic data makes these diagnostic criteria much more objective and selective than previous ones, namely the old Hachinski ischemic score (Hachinki et al., 1975), explaining why they have gathered more consensus in clinical practice, becoming the most widely used in research (Santana, 2006).

Vascular cognitive impairment and associated clinical features reflect the location, number, and extent of underlying ischemic, hemorrhagic, or hypoperfusion lesions (Desmond, 2004; Ueda et al., 1992). The ischemic forms of VaD are the most common and can be subclassified into large-vessel (where poststroke dementia is the most frequent form of VaD acute-onset) and small-vessel disease (Román, 2003). As a result of this heterogeneity in mechanisms, vascular territory involvement and location, cognitive impairment in VaD is highly variable and potentially affects all cognitive domains. Despite this, the preponderant neuropsychological features of VaD patients point to an overall profile of cognitive dysfunction that is frontally located in the brain, due to the early involvement of executive cortico-subcortical circuits (O´Brien et al., 2003; Román, 2003; Román & Royall, 1999; Santana, 2006). Executive impairment encompasses planning and sequencing, speed of mental processing, performance on unstructured tasks, verbal fluency and attention deficits (Desmond, 2004). Additionally, cortical functions such as language, calculation, and orientation tend to be relatively preserved, in contrast with AD patients (Desmond, 2004; Looi & Sachdev, 1999; Román & Royall, 1999). Deficits in recent episodic memory are usually less severe in VaD patients than in degenerative dementias, while concentration difficulties, working memory dysfunction, and psychomotor slowing are early and prominent symptoms in VaD (Looi & Sachdev, 1999; O´Brien et al., 2003; Román, 2003; Román & Royall, 1999). Other clinical features useful in the differential diagnosis with cortical degenerative dementia, namely AD, are the following: 1) sudden or gradual onset; 2) slow and stepwise progression, temporally related to ischemic

events; 3) presence of fluctuations (in cases with gradual onset); 4) presence of focal motor-sensitive-sensory signs noted during the physical examination; 5) early incontinence; and 6) disturbed gait, typically with short and shuffling steps (Román, 2003; Santana, 2006).

The high prevalence of VaD, the necessity of prevention strategies targeting vascular risk factors, and the recent advances of pharmacological treatments highlight the importance of an accurate screening method for this form of dementia, especially in the early stages. The Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) is the most widely used cognitive screening instrument for dementia, despite its well-known limitations; namely, it has low sensitivity to milder forms of cognitive impairment and does not evaluate executive functioning (Freitas, Santana, & Simões, 2010; Ihl, Frölich, Martin, & Maurer, 1992; Tombaugh & McIntyre, 1992; Wind et al., 1997). These issues, according to several experts, are especially relevant for dementias such as VaD that present prominent executive impairment (Hachinski et al., 2006; Martinić-Popović, Šerić, & Demarin, 2006; Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010; Pirscoveanu et al., 2009; Román, 2003; Román & Royall, 1999).

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a cognitive screening test specifically developed for the screening of milder forms of cognitive impairment. Surpassing the limitations of the MMSE and proving be a more useful, sensitive and accurate measure, the MoCA is now recognized as one of the best cognitive screening tests (Gauthier et al., 2011; Ismail, Rajji, & Shulman, 2009; Jacova, Kertesz, Blair, Fisk, & Feldman, 2007; Lonie, Tierney, & Ebmeier, 2009). Currently, the MoCA is an extensively validated screening tool for many disorders; it displays good overall psychometric properties and improved sensitivity to cognitive decline, which contributed to its rapid international recognition. This improved sensitivity in relation to other measures is related to the MoCA's more comprehensive assessment of major cognitive domains, including executive function, short-term memory, languages abilities, and visuospatial

processing. Considering the qualities and adequacy of the MoCA, the neuropsychology working group of the NINDS-CSN VCI Harmonization Standards criteria (Hachinski et al., 2006), recommends using the abbreviated version of the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) for brief cognitive screening in vascular patients in special settings such as primary health care, large epidemiological studies or clinical trials. This proposed *5-minute protocol* may be administered by telephone and is composed of three subtests: a five-word immediate and delayed recall test, a six-item orientation task, and a phonemic fluency test.

Several studies have been conducted to investigate cerebrovascular and cardiovascular diseases using the MoCA full version, namely in patients with Transient Ischemic Attack and Stroke (Cumming, Bernhardt, & Linden, 2011; Dong et al., 2010; Martinić-Popović et al., 2006; Martinić-Popović, Šerić, & Demarin, 2007; Pendlebury et al., 2010; Pirscoveanu et al., 2009), Cerebral Small-Vessel disease (Wong et al., 2009), confluent white matter lesion (Wong et al., 2008), and in rehabilitation settings (Aggarwal & Kean, 2010). All of these studies indicate that the MoCA is a psychometrically valid, reliable and sensitive cognitive screening test for the mentioned clinical conditions. Thus far, however, there have been neither studies of 'pure' VaD patients nor studies of the MoCA short version's validity.

The aim of the present study was to investigate the validity of the MoCA (Nasreddine et al., 2005; Simões et al., 2008) for cognitive screening of VaD patients. The psychometric properties and diagnostic accuracy of the MoCA was analyzed and the optimal cut-off points to detect VaD patients were established. Concurrently, the same analysis was conducted for the short version of the MoCA proposed by NINDS-CSN VCI Harmonization Standards (Hachinski et al., 2006). Furthermore, we also aimed to investigate the cognitive performance of the VaD patients on the MoCA's cognitive domains and analyze the differences with comparison to AD patients.

METHODS

Participants and Procedures

The study sample was composed of 102 participants distributed between three subgroups: (I) a VaD group with 34 patients, (II) an AD group with 34 patients, and (III) a Control group with 34 cognitively healthy adults. The demographic data of the participants in each group are summarized in Table 1.

The VaD patients were recruited between January 2009 and June 2011 at the Dementia Clinic of the Neurology Department of Coimbra University Hospital (Coimbra, Portugal) and included only patients with a diagnosis of probable VaD, based on international criteria (Román et al., 1993). Patients with Vascular Mild Cognitive Impairment (vMCI), also called Vascular Impairment no Dementia (VCIND), or with mixed dementia were not included. Eligibility was based on a comprehensive clinical evaluation, which included a neuropsychological and imaging study, and the final diagnosis was established by a multidisciplinary team consensus.

The AD group included the patients with a diagnosis of probable AD, as previously established by a multidisciplinary team consensus using international criteria (APA, 2000; McKhann et al., 1984). This diagnosis subgroup excluded patients with significant vascular disease, using either clinical or imaging evaluations. This group was selected from among the AD patients of the Dementia Clinic of the Neurology Department of Coimbra University Hospital (Coimbra, Portugal), in order to match VaD patients on gender, age, educational level, and severity of cognitive decline, as assessed by the MMSE (Folstein et al., 1975).

All patients were clinically examined by a neurologist (IS), and a standard investigation was always performed, including routine laboratory exams and analyses (Apolipoprotein E (APOE) genotyping and imaging studies: structural (CT and/or MRI) and functional (SPECT)). PET and cerebrospinal fluid analyses were carried out more restrictively, although they were considered in younger patients. Structural imaging studies,

namely CT or MRI, were fundamental in the differential diagnosis of dementia patients in this study. In accordance with the inclusion criteria for VaD and the exclusion criteria for AD, the following findings were relevant: evidence of large cortico-subcortical infarcts; extensive subcortical white matter lesions, greater than 25%; uni- or bilateral thalamic lacunes; lacune in the head of the caudate nucleus or in the inferior genu of the internal capsule; and more than 2 lacunes. At the outset of this study, the following were also considered exclusion criteria for patients' selection: 1) a unstable clinical condition, with significant comorbidities; 2) high dementia severity (only including patients with CDR ≤ 2 and MMSE ≥ 12 points); 3) recent pharmacotherapy changes; 4) recent psychiatric comorbidity (clinically diagnosed in the 6 months prior to the current neuropsychological evaluation); and 5) significant motor, visual or auditory deficits, all of which may influence neuropsychological assessment. For each patient considered suitable for the study at the time of data collection, a diagnosis was recorded in the clinical file by the neurologist.

All patients also underwent a comprehensive neuropsychological assessment battery including the following instruments: the MMSE (Folstein et al., 1975; Guerreiro, 1998), the Alzheimer´s Disease Assessment Scale (ADAS; Rosen, Mohs, & Davis, 1984; Guerreiro, Fonseca, Barreto, & Garcia, 2008), the Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982; Garret et al., 2008), the Irregular Word Reading Test (TeLPI; Alves, Simões, & Martins, 2009) for an estimate of pre-morbid intelligence, the Subjective Memory Complaints scale (SMC; Schmand, Jonker, Hooijer, & Lindeboom, 1996; Ginó et al., 2008), and the Geriatric Depression Scale (GDS-30; Yesavage et al., 1983; Barreto, Leuschner, Santos, & Sobral, 2008). The MoCA was never used for diagnostic purposes.

The control group was composed of cognitively healthy members of the community, living in Portugal. This group was selected from the database of the MoCA's normative study for the Portuguese population in

order to match each patient on variables that were found to be predictive of the MoCA´s performance (educational level and age; Freitas, Simões, Alves, & Santana, 2011), and additionally on gender. Details of the controls' recruitment procedure, inclusion and exclusion criteria, and neuropsychological assessment have been described in a previous study (Freitas et al., 2011).

An informed consent was obtained from all the participants after the research aims, procedures, and confidentiality requirements were fully disclosed by a member of the research team. For the patients who were not capable of providing the informed consent, a legal representative fulfilled that requirement on their behalf. The present research complied with the ethical guidelines for human experimentation stated in the Declaration of Helsinki and was approved by the Ethics Board of Coimbra University Hospital, by the "Fundação para a Ciência e Tecnologia" [Portuguese Foundation for Science and Technology] and by the Faculty of Psychology and Educational Sciences Scientific Committee.

Material and Neuropsychological Testing

Each participant was assessed in a single session by an expert in neuropsychology. In the clinical interview, the demographic and clinical data were collected through a complete sociodemographic questionnaire, an inventory of past habits and of the current clinical health status as well as of the medical history. Following this, the same neuropsychologist administered the MMSE (Folstein et al., 1975; Guerreiro, 1998) and the MoCA (Nasreddine et al., 2005; Simões et al., 2008), in that fixed order, to all subjects. The MMSE is a widely recognized and used brief screening instrument for cognitive decline, and therefore, it is not described in detail here. Both the MMSE and the MoCA are in paper-and-pencil format and are scored out of a possible total of 30 points, with higher scores indicating better cognitive performance. The MoCA was developed to screen milder forms of cognitive impairment through the assessment of six cognitive

domains: 1) executive functions; 2) visuospatial abilities; 3) short-term memory; 4) language; 5) attention, concentration and working memory; and 6) temporal and spatial orientation (Nasreddine et al., 2005). It is composed of a one-page test, with an administration time of approximately 10 to 15 minutes; a manual containing explicit instructions for administration and scoring is available. In the current study, the MoCA's total score refers to the raw score without any correction points for education effects, in contrast with the original study (Nasreddine et al., 2005); this correction is not used in the Portuguese population (Freitas et al., 2011).

Statistical Analysis

Statistical analyses of the data were carried out using the Statistical Package for the Social Sciences (SPSS, version 19.0) (IBM SPSS, Chicago, IL). Descriptive statistics were used for the sample's characterization. The χ^2 test, the two-sample *t*-test, the one-way between-groups analysis of variance (ANOVA), and the Tukey HSD and Bonferroni post-hoc test were conducted to explore group differences. The Cronbach´s alpha was considered as an index of internal consistency. The Pearson correlation coefficients were used for analyses of inter-rater reliability and convergent validity, and to explore the correlations between items, cognitive domains and total scores.

The diagnostic accuracy of the MoCA and the MMSE for the prediction of the clinical diagnosis of VaD was assessed through the receiver operating characteristics (ROC) curve analysis, implemented in MedCalc (version 11.6) (MedCalc Software, Mariakerke). In this analysis, the areas under the curve (AUC) can vary between 0.5 and 1, with larger AUC indicating better diagnostic accuracy. The ROC curves were compared according to the AUC comparison method of Hanley and McNeil (1983). The optimal cut-off points for each screening instrument that yielded the highest Youden index were selected, with higher Youden indices indicating maximum sensibility and specificity. To analyze the predictive value of the

tests, for each cut-off point, we calculated the sensibility (the probability of subjects with cognitive impairment having a positive result), specificity (the probability of subjects without cognitive impairment having a negative test), positive predictive value (PPV, the probability of disease in subjects with a positive result), negative predictive value (NPV, probability of a "lack of disease" classification in subjects with a negative result) and classification accuracy (probability of correct classification of subjects, with or without cognitive impairment).

RESULTS

Sample Characterization

The characteristics of the study sample, and in more detail of all subgroups, are presented in Table 20. For this description, were considered: sample size, gender, age, educational level, MMSE score and MoCA score.

Table 20. Demographic and clinical characteristics of the subgroups.

	VaD	AD	Control
n	34	34	34
Gender	12 (35.3)	12 (35.3)	12 (35.3)
Age	73.21 ± 7.85	74.00 ± 7.36	73.65 ± 7.40
Educational Level	4.97 ± 2.747	5.09 ± 2.54	5.09 ± 2.82
MMSE score	24.06 ± 4.01	23.24 ± 4.21	27.94 ± 1.41
MoCA score	13.06 ± 4.62	11.47 ± 4.24	22.97 ± 3.38

Abbreviations: VaD = group of patients with Vascular dementia; AD = group of patients with Alzheimer´s disease; Control = group of cognitively healthy adults; MoCA = Montreal Cognitive Assessment (maximum score = 30); MMSE = Mini Mental State Examination (maximum score = 30).

Note: Gender is characterized by female's *n* and respective percentage (%). Data of others variables are presented as mean ± standard deviation.

As mentioned above, the participants in the three groups were matched based on gender, age, and educational level. Additionally, the VaD and AD patients were also matched based on their MMSE scores. In fact, as seen on Table 1, there are no gender differences between the three groups. Likewise, no statistically significant differences were found based on age ($F_{(2,99)}$ = .095, p = .910) or educational level ($F_{(2,99)}$ = .021, p = .979). Furthermore, statistically significant differences in MMSE scores were not observed between clinical groups ($t_{(66)}$ = .826, p = .412), which suggests similarities in terms of cognitive decline severity.

Psychometric Properties

Cronbach´s alpha of the MoCA as an index of internal consistency was .908 for the total study sample, confirming the overall reliability of the scale when used to examine Portuguese subjects. Regarding the analysis of MoCA items that could be eliminated to increase consistency, the results indicated that none should be excluded. This reliability coefficient was also computed for each clinical group: α (VaD) = .825 and α (AD) = .806. The respective values for the MMSE were: α (total sample) = .807, α (VaD) = .771, and α (AD) = .804. The correlations between the MoCA scores and the MMSE scores were significant and positive in the total sample (r = .741, p < .001) and in the VaD group (r = .782, p < .001), which is indicative of convergent validity. The correlations between each item and the cognitive domains, as conceptualized by the original authors (Nasreddine et al., 2005), and between each cognitive domain and the MoCA total score were also explored in the VaD group. We found a significant (p < .001) and positive correlation between each cognitive domain and the total score of the scale (ranging from .495 to .780), which is suggestive of construct-related validity. Furthermore, we can observe that each domain showed significantly higher correlation with the MoCA total score than with another domain, which is suggestive of discriminative power of domains when used to examine VaD patients. Regarding the correlation coefficients of each item

within the cognitive domains, overall items showed a significantly higher correlation with the respective domain compared to the correlations with any other domain. The exceptions are the camel, second subtraction, place, and city items, which showed no significant correlation with any domain due to the lower variance of the results (hit rates: camel = 79.4; second subtraction = 23.5; place = 97.1; city = 100). Furthermore, the cube's copy showed a significant and similar correlation with the visuospatial domain (r = .452, p < .001) and with the executive function domain (r = .491, p < .001).

Group Differences

Comparing the MoCA total scores of the three groups, statistically significant differences can be observed ($F_{(2,99)}$ = 78.121, p < .001). However, according to *post-hoc* tests, these differences occurred between the control group and both clinical groups, with higher performance seen in the healthy participants. No differences were found between VaD and AD groups, which were previously matched based on their MMSE scores. As expected, a more detailed analysis regarding sub-scores of the MoCA cognitive domains revealed that the healthy participants had higher performances in all cognitive domains than both clinical groups. However, there were no statistically significant differences between the VaD and AD patients at the level of the cognitive domains of the MoCA, nor at the level of some tasks' sub-scores, such as clock drawing, naming tasks, subtraction, and abstraction tasks. Additionally, no differences in the number of the words stated in the phonemic fluency task were found.

Considering the abbreviated version of the MoCA proposed by the NINDS-CSN VCI Harmonization Standards criteria (Hachinski et al., 2006) as a *5-minute protocol* (total score = 12), no statistically significant differences were found between VaD (5.50 ± 1.93) and AD patients (4.65 ± 1.89). Nevertheless, the short version of the MoCA discriminates control subjects (9.32 ± 1.408) from both clinical groups, according to the post-hoc tests ($F_{(2,99)}$ = 68.295, p < .001).

Cut-off points

The receiver operating characteristics (ROC) curve analysis and the predictive values were computed to evaluate the diagnostic accuracy of MoCA to discriminate VaD patients from cognitively healthy adults. First, the diagnostic accuracy of the MoCA full version was compared with the diagnostic accuracy of the MMSE; then, the MoCA full version was compared with the short version (Hachinski et al., 2006).

The MoCA discriminant potential for VaD was excellent, with an AUC of .950 (95% confidence interval = .868 - .988), while the MMSE demonstrated an AUC of .860 (95% confidence interval = .754 - .932). These AUCs are significantly different (z = 2.142, p = .0322), according to the AUC comparison method of Hanley and McNeil (1983), indicating different classificatory accuracy of the instruments. Graphic representations of the ROC curves are provided in Figure 4.

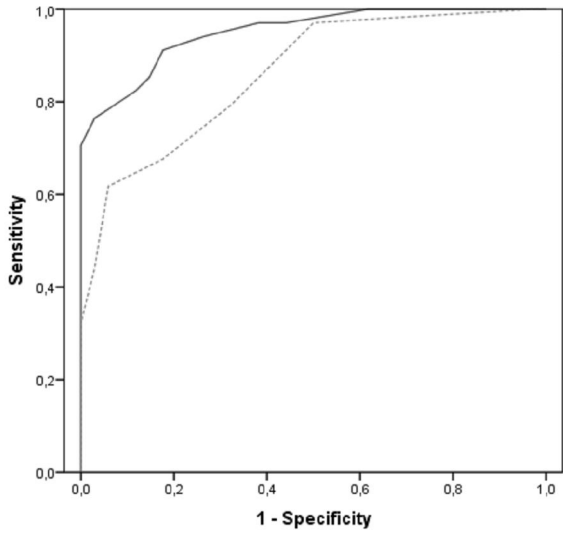

Figure 4. ROC curve analysis of the MoCA total scale (continuous line) and MMSE (dashed line) to detect VaD patients.

Abbreviations: MoCA: Montreal Cognitive Assessment; MMSE: Mini Mental State Examination; VaD: Vascular dementia.

It can be observed that the MoCA's ROC curve fully includes the curve for the MMSE; this is a clear indication that there is always a cut-off for the MoCA, with higher sensitivity and specificity, for any cut-off chosen for the MMSE. The optimal cut-off point for maximum accuracy (Youden index) and the respective values of sensitivity, specificity, PPV, NPV, and classification accuracy are described for both instruments in Table 21.

Comparing the AUCs of the MoCA full and short versions (AUC = .936; 95% confidence interval = .849 - .981), no statistically significant differences were found (z = .488, p = .6256), according to the AUC comparison method of Hanley and McNeil (1983). Graphic representations of the ROC curves are provided in Figure 5; the optimal cut-off point for maximum accuracy (Youden index) and the respective values of sensitivity, specificity, PPV, NPV, and classification accuracy of the MoCA short version are also presented in Table 21.

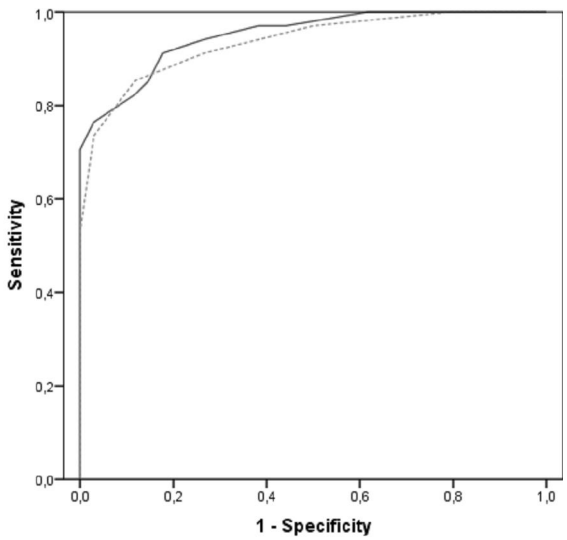

Figure 5. ROC curve analysis of the MoCA total scale (continuous line) and MoCA short version (dashed line) to detect VaD patients.

Abbreviations: MoCA: Montreal Cognitive Assessment; MMSE: Mini Mental State Examination; VaD: Vascular dementia.

Table 21. Diagnostic accuracy of the MoCA full version, MoCA short version and MMSE to VaD

	Cut-off	Sensitivity	Specificity	PPV	NPV	Classification Accuracy
MoCA Full Version	< 17	77	97	96	81	87
MoCA Short Version	< 8	85	88	88	86	87
MMSE	< 26	62	94	91	71	78

Abbreviations: MoCA: Montreal Cognitive Assessment (maximum score = 30); MoCA Short Version: abbreviated version proposed by the NINDS-CSN VCI Harmonization Standards criteria (maximum score = 12); MMSE: Mini Mental State Examination (maximum score = 30); AUC: area under the operating characteristic curve; PPV: positive predictive value; NPV: negative predictive value.

Note 1: Sensitivity, Specificity, PPV, NPV, and Classification Accuracy values were expressed in percentage.

Note 2: Cut-off values indicate the minimum score required for absence of signal.

DISCUSSION

Accurate screening of the early stages of VaD assumes extreme importance, considering the high prevalence rates of vascular cognitive impairment and the available primary and secondary prevention strategies. The MMSE reveals limitations in effective cognitive assessment of patients with VaD because it does not include tasks for the evaluation of the main area of compromise: executive dysfunction. Thus, this study aims to validate the MoCA, as well as the short version of the MoCA proposed by NINDS-CSN VCI Harmonization Standards, as a *5-minute protocol* for cognitive screening of VaD patients.

Due to the clinical heterogeneity of the VCI conditions, this investigation was carried out in a homogeneity sample of VaD patients. Patients who did not meet the criteria for dementia or with mixed dementia classification were excluded. The rigorous procedures adopted by the

multidisciplinary team ensure the correct diagnosis of patients according to the international criteria for VaD (Román et al., 1993). Major methodological strengths are the comprehensive clinical evaluation with routine laboratory exams, strict and rigorous imaging inclusion criteria, a comprehensive neuropsychological assessment battery, and several exclusion criteria for patients' selection at the outset. Although some studies conducted in cerebrovascular and cardiovascular patients (Aggarwal & Kean, 2010; Cumming et al., 2011; Dong et al., 2010; Martinić-Popović et al., 2006; Martinić-Popović et al., 2007; Pendlebury et al., 2010; Pirscoveanu et al., 2009; Wong et al., 2009) support the validity, reliability and sensitivity of the MoCA, we are aware of neither previous studies using 'pure' VaD patients to confirm those results nor studies of validation of the MoCA short version.

The results of the present study demonstrate that the MoCA is a psychometrically valid and reliable instrument for the cognitive screening of VaD patients. The internal consistency measured by Cronbach's alpha was high, confirming the overall reliability of the scale when used to examine Portuguese VaD patients. Furthermore, the significant and positive correlations between the MoCA scores and the MMSE scores are suggestive of convergent validity. On the other hand, the significant and positive correlations between each cognitive domain, as conceptualized by the original authors (Nasreddine et al., 2005), and the MoCA total score are suggestive of construct-related validity; the higher correlations between each cognitive domain and the MoCA total score compared with other domains, however, are suggestive of the discriminative power of domains when used to examine VaD patients. Finally, items showed a significantly higher correlation with their respective domains compared with other domains, with the exception of camel, second subtraction, place, and city items; these showed no significant correlation with any domain, possibly due to the lower variance of the items in this sample. Furthermore, we hypothesize that the significant correlation found between the cube's copy item and executive function domain, beyond its correlation with the visuospatial domain, is

explained by the three-dimensional nature of the drawing; it involves the use of planning, sequencing and attentional skills.

For the MoCA's discriminant capacity analysis, participants in the three groups (VaD, AD, and controls) were matched for gender, age, and educational level; the two clinical groups were also matched based on MMSE scores to ensure comparable levels of severity of cognitive decline. The results showed that both the full and short versions of the MoCA efficiently discriminate the cognitively healthy adults from both clinical groups. However, no statistically significant differences were found between VaD and AD patients using both MoCA versions. Additionally, no differences were found between VaD and AD patients' performances in the different cognitive domains of the MoCA, or at the level of some tasks' sub-scores (clock drawing, naming tasks, subtraction, and abstraction tasks). However, performance of the healthy participants in all cognitive domains was significantly higher than that of both clinical groups. We think that the methodological decision of matching the clinical groups in terms of cognitive severity level, as assessed by the MMSE, may have contributed to this undifferentiated neuropsychological performance. Furthermore, it is important to note that a number of prior studies have failed to identify significant differences in neuropsychological performance between VaD and AD patients (Desmond, 2004; Braaten, Parsons, McCue, Sellers, & Burns, 2006). On the other hand, the MoCA's sensitivity and discriminant capacity at level of cognitive domains were well-demonstrated in three validation studies developed by our research group (Freitas, Simões, Marôco, Alves, & Santana, 2011; Freitas, Simões, Alves, & Santana, 2012; Freitas, Simões, Alves, Duro, & Santana, *submitted*). This was the case for the comparative analysis of Frontotemporal Dementia (behavioral-variant) and AD (Freitas, Simões, Alves, Duro, & Santana, *submitted*), where we observed significant differences in MoCA total scores and in the sub-scores of the short-term memory and visuospatial domains, showing lower performance by AD patients. The undifferentiated performance founded may reflect the close

cognitive profile between VaD and the AD patients more so than the instrument's inability to capture cognitive profiles.

The MoCA scores also displayed excellent diagnostic accuracy in the discrimination of VaD symptoms from age-related changes in cognitively healthy elderly adults, exhibiting an AUC significantly higher than that of the MMSE's AUC; this confirms the superior classificatory accuracy of the MoCA. The optimal cut-off point on the MoCA for VaD patients, allowing maximum sensibility and specificity, was below 17 points. This cut-off point is equivalent to the optimal cut-off for AD, as established by our previous validation study (Freitas, et al., 2012), as well as for Frontotemporal Dementia - behavioral-variant patients (Freitas, Simões, Alves, Duro, & Santana, *submitted*). With this cut-off point, the MoCA showed good sensitivity (77%), excellent specificity (97%) and PPV (96%), and good NPV (81%) and classification accuracy (87%). With an optimal cut-off point of below 26 points, the MMSE had consistently lower respective values, namely in sensitivity (62%) and classificatory accuracy (78%); this suggests that the MMSE is not a good option as cognitive screening instrument for VaD, as some authors have claimed (Hachinski et al., 2006; Moorhouse & Rockwood, 2008; Pendlebury et al., 2010; Román, 2003). The main reasons for the MoCA's higher results at this level were the inclusion of the executive function assessment and the consideration of more complex tasks to measure short-term memory, language, attention, concentration, working memory, and visuospatial skills.

The MoCA's short version, proposed by NINDS-CSN VCI Harmonization Standards (Hachinski et al., 2006) as a *5-minute protocol*, also demonstrated excellent diagnostic accuracy in discriminating VaD patients from the control participants. With an optimal cut-off point of below 8 points, this abbreviated version showed high sensitivity (85%), specificity (88%), PPV (88%), NPV (86%), and classification accuracy (87%). No significant differences were found in comparison with the MoCA full version;

thus, it is a valid abbreviated option, useful in clinical settings with time constraints.

The main strengths of this study are: 1) the homogeneity of the VaD group; 2) the homogeneity of the samples in terms of group size, gender, age, educational level and severity of cognitive decline in the clinical groups, which allowed a more clear analysis and minimized the influence of individual and methodological variables; 3) the above-mentioned rigorous procedures adopted to ensure a probable diagnosis of VaD and AD; 4) the well-characterized control group, composed of cognitively healthy adult members of the community; and 5) the reduction of inter-rater variability because all participants were assessed by one of two expert neuropsychologists.

Some limitations of this study must be addressed, however. First of all, as we intended to include and obtain results from 'pure' VaD patients, the generalization of these results to other VCI subtypes should be performed with caution. Another point to mention is that the scores of the MoCA short version were computed after the complete administration of the MoCA, rather than resulting from second separate administration. Finally, because this is the first study of its kind to validate the MoCA full and short versions for the screening of VaD patients, a comparative analysis with other studies cannot be performed.

In conclusion, the MoCA full and short versions proved to be valid, reliable, sensitive and accurate measures of cognitive impairment in VaD. Compared with the widely used MMSE, this study produced evidence of the overall superiority of both MoCA versions in terms of diagnostic accuracy, confirming its great potential and usefulness for the brief cognitive assessment of VaD patients.

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ESTUDO VII

Montreal Cognitive Assessment (MoCA): Normative study for the Portuguese population

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Abstract

The MoCA is a brief cognitive screening instrument with good psychometric features and an excellent sensitivity in the early detection of mild cognitive decline. The MoCA was applied to a community-based sample of cognitively healthy adults (*n* = 650), stratified according to sociodemographic variables (age, gender, educational level, geographic region, geographic localization and residence area), with a distribution similar to that observed in the Portuguese population. The normative data were determined according to age and education as these were the sociodemographic variables that most significantly contributed to the prediction of the MoCA scores, explaining 49% of their variance.

Keywords: norms; cognitive screening; Mild Cognitive Impairment; Alzheimer's disease.

INTRODUCTION

One of the most significant demographic changes of recent decades is the decline of birth rates and the increase in life expectancy. Demographic aging is a reality and the proportion of elders has increased rapidly in most countries (Federal Interagency Forum on Aging-Related Statistics, 2000), including in Portugal (European Commission, 2010; Instituto Nacional de Estatística, 2004, 2009). Aging is a major risk factor for dementia and its most common form, Alzheimer's disease (AD) (Barranco-Quintana, Allam, Castillo, & Navajas, 2005; Chen, Lin, & Chen, 2009; Herrera-Rivero, Hernández-Aguilar, Manzo, & Aranda-Abreu, 2010; Luck, Luppa, Briel, & Riedel-Heller, 2010; Seshadri et al., 1997). Epidemiological studies indicate that rates of AD incidence and prevalence increase with aging, almost doubling every five years after the sixth decade of life (Ferri et al., 2005; Jorm, Korten, & Henderson, 1987; McDowell, 2001; Wimo, Winblad, Aguero-Torres, & von Strauss, 2004). In this context, in which dementia has a significant impact on worldwide public health (Comas-Herrera et al., 2011; Federal Interagency Forum on Aging-Related Statistics, 2010; Langa et al., 2001; World Health Organization, 2003), early diagnosis and screening for cognitive impairment are extremely important. The cognitive screening tests remain the best method for the early detection of dementia in population studies (Cullen, O'Neill, Evans, Coen, & Lawlor, 2007; Ismail & Shulman, 2006), allowing the identification of individuals in preclinical stages (Fabrigoule, Barberger-Gateau, & Dartigues, 2006). However, the results of these evaluations can be compromised by deficient translations or cultural background adaptations, and lack of psychometric validation of the instruments used.

The *Montreal Cognitive Assessment* (MoCA) (Nasreddine et al., 2005; Simões et al., 2008) was specifically developed for the screening of Mild Cognitive Impairment (MCI), an intermediate clinical state between normal cognitive aging and dementia that often precedes and leads to dementia (Cargin, Maruff, Collie & Masters, 2006; Gauthier et al., 2006;

Petersen, 2000, 2003, 2004, 2007; Petersen et al., 2001; Winblad et al., 2004). The MoCA is a one-page test with a maximum score of 30 points and it assesses eight cognitive domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration and working memory; and temporal and spatial orientation (Nasreddine et al., 2005). The results of several studies (see studies in http://www.mocatest.org) show that the MoCA has good psychometric features and excellent sensitivity, with better results than the widely used *Mini-Mental State Examination* (MMSE; Folstein, Folstein & McHugh, 1975) in the early identification of cognitive decline in course of the disease. The use of the MoCA is widespread, having been adapted and validated in 34 countries for several pathologies (see also http://www.mocatest.org), and it has become one of the preferred brief screening tests (Appels & Scherder, 2010; Ismail, Rajji & Shulman, 2009; Jacova, Kertesz, Blair, Fisk & Feldman, 2007; Lonie, Tierney & Ebmeier, 2009).

The MoCA was translated, adapted and validated for Portuguese population by our group (Freitas, Simões, Martins, Vilar, & Santana, 2010), and has been widely used in clinical practice and in research. Despite previous results supporting the excellent psychometric features and discriminant validity of the MoCA Portuguese final version, its clinical value is restricted by the lack of normative data. The main objective of this study was to obtain the MoCA's normative data for the Portuguese population. Norms allow interpreting test performance in comparison with a reference group. We also wanted to confirm the applicability of the MoCA in this cultural context and to evaluate the influence of the sociodemographic characteristics on the MoCA's performance. For this, we used a large Portuguese community-based sample stratified according to sociodemographic variables.

METHOD

Study population

A community-based sample of volunteers aged 25 years and older, living in all geographic regions of the Portuguese continental territory, and representative of the Portuguese population, was recruited at national health and social security services. Several demographic and clinical inclusion criteria were considered in the initial subject selection: age 25 years and older; Portuguese as their native language and schooling in Portugal; absence of significant motor, visual or auditory deficits, all of which may influence performance on tests; and to ensure that participants were cognitively healthy adults: autonomy in daily living activities; no history of alcoholism or substance abuse; absence of neurological or psychiatric diseases, as well as of chronic unstable systemic disorders with impact in cognition; absence of significant depressive complaints and medication with possible impact in cognition (e.g., psychotropic or psycho-active drugs). In order to implement and confirm these general criteria, the recruited subjects were interviewed by a psychologist with a standard questionnaire including a complete sociodemographic questionnaire, an inventory of current clinical health status, and past habits and medical history. In case of older participants, this information was always also checked with general practioner, community center directors and/or an informant, usually an individual in co-habitation or a close relative. For further inclusion in the study, all the subjects were required to display normal performance on others tools of the assessment battery especially composed for this study and with accessible Portuguese-validated data (see “Materials and procedures”). The study was approved by the Fundação para a Ciência e Tecnologia [Portuguese Foundation for Science and Technology] and by the Faculty of Psychology and Educational Sciences Scientific Committee and an informed consent was obtained from all the participants after the aims and procedures of the investigation were fully explained by a member of the study group.

From the initial community-based sample of the 936 volunteers, 194 (20.73 %) were excluded after the interview (most frequent reasons were history of neurological or psychiatric disorder and history of alcohol abuse), and 92 (9.83 %) were excluded because of their performance on the assessment battery, suggesting the presence of cognitive impairment or depressive symptoms according to Portuguese cutoff points. The final sample is composed by 650 cognitively healthy adults that met all the inclusion criteria defined. The stratification according to sociodemographic variables confirmed that this final sample was representative of the distribution observed in the Portuguese population.

Materials and procedures

All participants were assessed by two psychologists with expertise in neuropsychological assessment. Besides the Portuguese final version of MoCA , the following instruments were administered for a global assessment of each participant: a complete sociodemographic questionnaire; an inventory of current clinical health status, and past habits and medical history; MMSE (Folstein et al., 1975; Guerreiro, 1998); Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben & Martin, 1982; Garret et al., 2008) (only for participants above 49 years); Irregular Word Reading Test (TeLPI: Teste de Leitura de Palavras Irregulares; Alves, Simões & Martins, 2009) for pre-morbid intelligence estimation; Subjective Memory Complaints scale (SMC; Schmand, Jonker, Hooijer & Lindeboom, 1996; Ginó et al., 2008); and Geriatric Depression Scale (GDS-30; Yesavage et al., 1983; Barreto, Leuschner, Santos & Sobral, 2008). As mentioned, sociodemographic and clinical data were obtained directly from the cognitively healthy subjects and corroborated by a third party in case of the older participants. The autonomy in daily life activities was assessed through the CDR and supplemented with the interview with the subject and with information obtained through general practioner, community center directors and/or an informant. The depressive complaints were measured trough

clinical interview and Geriatric Depression Scale, been excluding subjects with score 20 or more points.

Sociodemographic variables

The sample of 650 subjects was stratified according the following sociodemographic variables: age, gender, educational level, geographic region, geographic localization and residence area. The age intervals considered were the following: 25 – 49 (mean age = 38.12 ± 8.086), 50 – 64 (mean age = 57.12 ± 4.199), and 65 and over years of age (mean age = 71.96 ± 5.433). Four educational levels were considered, according to the number of school years successfully completed in the Portuguese education system: 1-4 (primary education), 5-9 (middle school), 10-12 (high school) and over 12 years of education (university/college), categories that match the divisions in the Portuguese school system. The Portuguese continental territory is divided into five geographic regions (NUTS II classification): North, Centre, Lisbon, Alentejo and Algarve; furthermore, two geographic localizations were considered: coast and inland (Instituto Nacional de Estatística, 2010). The residence area, which was categorized according to the Types of Urban Areas (Instituto Nacional de Estatística, 2010), was divided into predominantly urban areas (PUA), moderately urban areas (MUA) and predominantly rural areas (PRA).

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 17.0. Firstly, differences in the MoCA scores among subgroups stratified according to sociodemographic variables were examined using Student's *t*-test, analysis of variance (ANOVA), and Tukey post-hoc test. The influence of geographic regions and residence area on the MoCA scores, considering the influence of age and education, was addressed with the analysis of covariance (ANCOVA). Eta squared (η^2) was used as an estimate of the effect size (Cohen, 1988). The correlation

between the MoCA scores, age and education was investigated with the Pearson correlation coefficient (*r*) (Cohen, 1988). Multiple Linear Regression (MLR) analysis, using the enter method, was performed to examine the significance of age (in years), and education (years of schooling completed successfully) as influencing factors for the MoCA. The multicollinearity was examined through Tolerance and Variance Inflation Factor (VIF) statistics (Meyers, Gamst & Guarino, 2006). The coefficient of determination (R^2) was considered in the analysis of effect size in the regressions (Cohen, 1988). Finally, the norms of the MoCA were stratified and determined according to the sociodemographic variables most significantly associated with the MoCA scores. The normative data are expressed as the means ± standard deviations (S.D.s), and those of the distributions are given as means below 1S.D., 1.5S.D.s and 2S.D.s.

RESULTS

The final sample is composed of 650 participants (mean age = 55.84 ± 15.12, age range = [25-91]; mean education = 8.16 ± 4.72, education range = [2-27]). The sociodemographic characteristics of the study subjects are provided in Table 22. We can observe that the distribution of the sample in several strata is comparable to the distribution of the target Portuguese population. The participants' performance in others tools of the assessment battery are summarized in Table 23.

The MoCA showed internal consistency measured by a Cronbach alpha of 0.775, in this community sample. Furthermore, the analyses of the relationships between the MoCA score[3] and the sociodemographic variables showed that age ($F_{(2,647)}$ = 95.130, p <.001), educational level ($F_{(3,646)}$ = 194.996, p <.001), geographic region ($F_{(4,645)}$ = 8.765, p <.001), and residence area ($F_{(2,647)}$ = 4.175, p =.016) all had significant effects on the

[3] The total score of the MoCA refers to the real score without one correction point for education effects, considered in the original study (Nasreddine et al., 2005).

MoCA scores' distribution. There are no statistically significant differences in gender (t = 1.80, p = .072) or geographic localization (t = 1.546, p =.122).

Table 22. Sociodemographic characterization of the population sample

Variables	Levels	Sample	Portugal
		n (%)	*n* (%)
Age	25 - 49	214 (33.0)	-
	50 - 64	218 (33.5)	-
	≥ 65	218 (33.5)	-
Gender	Female	408 (62.8)	3 946 (52.6)
	Male	242 (37.2)	3 559 (47.4)
Educational Level	Primary	256 (39.4)	2 426 (36.6)
	Middle	170 (26.2)	2 280 (34.4)
	High	112 (17.2)	960 (14.5)
	University	112 (17.2)	956 (14.5)
Geographic Region	North	251 (38.6)	2 722 (36)
	Center	174 (26.8)	1 794 (24)
	Lisbon	164 (25.2)	2 091 (28)
	Alentejo	44 (6.8)	577 (8)
	Algarve	17 (2.6)	321 (4)
Geographic Localization	Coast	546 (84)	6 379 (85)
	Inland	104 (16)	1 126 (15)
Residence Area	PUA	446 (68.6)	5 103 (68)
	MUA	112 (17.2)	1 200 (16)
	PRA	92 (14.2)	1 200 (16)

Abbreviations: PUA = predominantly urban areas; MUA = moderately urban areas; PRA = predominantly rural areas.

Note: The values (*n*) of the Portuguese population are expressed in thousands and represent data of the resident population in continental Portugal aged over 24 years (Instituto Nacional de Estatística, 2010).

We found differences in mean-age and mean-education levels among subjects living in different geographic regions (age: $F_{(4,645)}$ = 6.507, p <.001; education: $F_{(4,645)}$ = 15.675, p <.001) and residence area (education: $F_{(2,647)}$ = 8,450, p <.001). We then proceeded to the analysis of covariance,

in order to examine whether differences on the MoCA scores remained significant after controlling the effect of covariates (age and education). The differences on the MoCA scores among subjects living in different residence areas were not sustained ($F_{(2,646)} = .122$, $p = .885$, $\eta_p^2 = .000$) and those among subjects living in different geographic regions showed a medium-low effect size ($F_{(4,643)} = 4.972$, $p = .001$, $\eta_p^2 = .030$).

Table 23. Performance of the population sample in battery assessment

Age Levels	CDR (*M*)	MMSE (*M* ± *SD*)	SMC (*M* ± *SD*)	GDS-30 (*M* ± *SD*)
25 - 49	0	29.47 ± 0.902	4.37 ± 3.627	6.59 ± 5.495
50 - 64	0	28.81 ± 1.266	6.21 ± 3.419	8.03 ± 5.384
≥ 65	0	28.39 ± 1.506	6.37 ± 3.398	7.36 ± 5.158

Abbreviations: CDR = Clinical Dementia Rating scale; MMSE = Mini Mental State Examination; SMC = Subjective Memory Complaints scale; GDS -30 = Geriatric Depression Scale, version 30 items

Multiple linear regression, using the enter method, was conducted to compare the independent influences of age and educational level on the MoCA scores and to examine the additional contributions of these significant variables and their interactions. Preliminary analyses were done to ensure no violation of the assumptions of normality, linearity, multicollinearity and homoscedasticity. The means, standard deviations, and intercorrelations can be found in Table 24. Both variables are significantly contributing to the prediction of the MoCA scores ($F_{(2,647)} = 317.016$, $p < .001$). The beta weights, presented in Table 25, suggest that educational level contributes most to predicting the MoCA scores and that age also contributes to this prediction. The adjusted *R* squared value is .49, which indicates that 49% of the variance on the MoCA scores was explained by the model.

Table 24. Means, Standard Deviation, and Intercorrelations for MoCA and Predictor Variables (*n* = 650)

Variable	*M*	*SD*	Age	Education
MoCA	24.70	3.668	-.522**	.652**
Predictor Variable				
Age	55.84	15.120	-	-.438**
Education	8.16	4.724		-

Note: *p < .05; **p < .01

Table 25. Multiple Regression Analysis summary for Age and Education predicting the MoCA scores

Variable	*B*	*SEB*	*β*
Age	-.07	.01	-.29**
Education	.40	.02	.52**

Note 1: R^2 = .49; $F_{(2,647)}$ = 317.016, p<.001

Note 2: *p < .05; **p < .01

According to results of the multiple linear regression analysis, age and education were considered in the development of the normative data of the MoCA for the Portuguese population. The normative data were determined and stratified according to the distributional properties of each variable. The MoCA scores are expressed as the means ± S.D.s, and those of the distributions which are below 1S.D., 1.5S.D.s and 2S.D.s., can be considered as cutoff points for possible cognitive impairment (Table 26).

Table 26. Normative data of the MoCA scores according to age and educational level

	Educational Level (years)				
Age	**Primary (1-4)**	**Middle (5-9)**	**High (10-12)**	**University (>12)**	**All education**
(*n*)	(29)	(66)	(59)	(60)	(214)
25-49	23.55 ± 2.56	26.42 ± 2.18	27.39 ± 1.86	28.83 ± 1.38	26.98 ± 2.55
***SD**	21 - 20 - 18	24 - 23 - 22	26 - 25 - 24	28 - 27 - 26	24 - 23 - 22
(*n*)	(91)	(59)	(33)	(35)	(218)
50-64	21.78 ± 2.86	25.58 ± 2.25	26.61 ± 2.28	27.51 ± 2.13	24.46 ± 3.43
***SD**	19 - 18 - 16	23 - 22 - 21	24 - 23 - 22	25 - 24 - 23	21 - 19 - 18
(*n*)	(136)	(45)	(20)	(17)	(218)
≥ 65	21.27 ± 3.37	24.60 ± 2.87	25.11 ± 1.94	26.35 ± 1.87	22.71 ± 3.60
***SD**	18 - 16 - 15	22 - 20 - 19	23 - 22 - 21	25 - 24 - 23	19 - 17 - 16
(*n*)	(256)	(170)	(112)	(112)	(650)
All age	21.71 ± 3.18	25.65 ± 2.50	26.77 ± 2.15	28.04 ± 1.94	24.70 ± 3.67
***SD**	19 - 17 - 15	23 - 22 - 21	25 - 24 - 23	26 - 25 - 24	21 - 19 - 17

* Note: MoCA values below 1S.D., 1.5S.D and 2S.D., respectively.

DISCUSSION

This study analyzes the influence of sociodemographic variables on MoCA performance and provides the norms of the MoCA according to age and educational level for the Portuguese population. The use of a representative sample stratified according to various levels of each sociodemographic variable with a distribution very close to that observed in

the Portuguese population enhances the equivalence with the target population and the confidence of the conclusions drawn. Age and educational level were the socio-demographic variables that more significantly contributed to the prediction of the MoCA scores, explaining 49% of the variance. This is considered a large effect, according Cohen (1988) and a respectable result according to Pallant (2007).

As expected, our results suggest that the total score on the MoCA consistently increases with the educational level and decreases as age progresses. According to previous studies of cognitive screening tests (Bravo & Hébert, 1997; Gallacher et al., 1999; Han et al., 2008; Langa et al., 2009; Lieberman et al., 1999; Mathuranath et al., 2007; Measso et al., 1993; Moraes, Pinto, Lopes, Litvoc & Bottino, 2010; Morgado, Rocha, Maruta, Guerreiro & Martins, 2010; Nguyen, Black, Ray, Espino & Markides, 2002), our results confirm that older age has a significant effect on MoCA performance, contributing to lower test scores. The influence of educational level on brief cognitive screening tests performance is also widely reported in the literature (Bravo & Hébert, 1997; Gallacher at al., 1999; Han et al., 2008; Langa et al., 2009; Lieberman et al., 1999; Mathuranath et al., 2007; Measso et al., 1993; Moraes et al., 2010; Morgado, Rocha, Maruta, Guerreiro & Martins, 2009; Morgado et al., 2010; Nguyen et al., 2002), with the worst performance in lower education levels and ceiling effects in highly educated individuals. The magnitude of this effect is so strong that education is invariably considered a criterion for the establishment of normative-data for cognitive tests (Bravo & Hébert, 1997; Guerreiro, 1998; Han et al., 2008; Mathuranath et al., 2007; Measso et al., 1993; Morgado et al., 2009). Because of the verified effect of education on the MoCA performance, Nasreddine and collaborators (2005) included a correction point for individuals with 12 or less years of education. However, for the Portuguese population, as it is characterized by a considerable lower education level than the original study population (mean education of Portuguese population = 8.16 ± 4.72; mean education of Canadian sample = 13.33 ± 3.40;

Nasreddine et al., 2005), the correction point is not integrally applicable because of these differences in education found between the two samples. This is an additional reason why in this study the norms for the Portuguese population were calculated and stratified according to the different educational levels.

The influence of gender in screening tests is more controversial in the literature. Some studies (Han et al., 2008; Bravo & Hébert, 1997; Measso et al., 1993) suggest the importance of this variable, while in other studies gender does not contribute significantly to data distribution (Lieberman et al., 1999; Mathuranath et al., 2007; Morgado et al., 2009). In our study, gender did not reveal a significant effect on MoCA results.

We are not aware of previous studies in Portugal where the influence of geographical variables on cognitive screening tests performance was evaluated. Our results indicate that there are no statistically significant differences between subjects living in the coastal and inland areas. Furthermore, the differences observed between residents in predominantly urban or rural areas were not significant after controlling for the effect of education. The observed differences between residents in different geographic regions also showed a reduced magnitude after controlling for age and education. In fact, these regional subgroups were not completely matched for age and education, which may explain the obtained results.

We determined the means and S.D. for each sub-group result from the crossing of the various educational and age levels. In addition, cutoffs of 1S.D., 1.5S.D. and 2S.D. were also used to define the norms. Several cutoff points were calculated because different cutoffs are presented in the literature, particularly in MCI studies. This study provides appropriate normative data for the MoCA, but we can't corroborate these data in other cultural-settings, as there are no equivalent international studies that analyze the influence of sociodemographic variables on MoCA's performance. Furthermore, in our country there are no studies with national representative samples using the MoCA or any other similar screening instrument. Recently

new MMSE´s normative data were established for the Portuguese population (Morgado et al., 2009) according to age and educational level, but the study's sample is exclusively composed of metropolitan area residents.

The main limitation of the present study was the exclusion of the illiterate subjects. The MoCA is a tool with a significant impact of literacy in the performance. Several MoCA's items are unsuitable for subjects without formal education. The maintenance of those items with a scoring of zero would impact in the global scoring with a strong floor effect and possible loss of sensibility to detect the cognitive impairment. Furthermore, the MoCA was developed for screening subjects with formal education, having not been covered illiterate subjects in the original study (Nasreddine et al., 2005) or in any other international study with the instrument. The adequate assessment of the illiterate subjects requires significant adaptation of the items for this context or tools specifically developed with this objective. Moreover, the impossibility to match all the age-subgroups in terms of education mean constitutes another limitation. The younger group shows higher education levels than the older group, which is representative of the demographic profile of our country, where, in the last decades, the educational scenery has rapidly changed as a result of the reorganization of the school system and the imposition of higher obligatory educational plateaus. These changes are already reflected in the younger strata of the population studied, however the older group continues to be characterized by a very low education level. As an illustrative example, 30 years ago, according to the 1981 Census (Instituto Nacional de Estatística, 2010), the percentage of analphabetism in Portugal was close to 26.4% and only 1.6% of the population held a university degree.

Our study stresses the importance of considering age and education influences on test performances and provides robust normative data for the MoCA. These reference values are useful in both clinical and research contexts, where the MoCA has been increasingly used to assess cognitive

dysfunction, and are furthermore a baseline reference for further normative studies in other countries.

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DISCUSSÃO GERAL

Discussão Geral

A Discussão Geral da presente dissertação pretende, de modo resumido, analisar alguns dos principais resultados obtidos no conjunto das investigações realizadas com o MoCA e anteriormente apresentadas sob a forma de artigos (publicados, aceites para publicação ou submetidos). Está organizada de acordo com as seguintes rubricas: *Fundamentação do projecto de investigação*, *Adaptação transcultural*, *Validação psicométrica*, *Validação clínica*, *Normas e influência de variáveis no desempenho*, *Pontos fortes e limitações*, *Estudos futuros* e *Conclusões*.

FUNDAMENTAÇÃO DO PROJECTO DE INVESTIGAÇÃO

Os dados demográficos disponíveis indicam que Portugal segue a tendência de **envelhecimento progressivo da população** observada nos países desenvolvidos ou em vias de desenvolvimento. Esta evolução demográfica acompanha-se de um **aumento da prevalência da demência e, em particular, da Doença de Alzheimer (DA)**. Neste contexto, reveste-se de especial importância a existência de **instrumentos de rastreio cognitivo adaptados à população portuguesa**, de fácil aplicação em todos os contextos clínicos, e que sejam úteis e eficazes na distinção entre as alterações cognitivas próprias do envelhecimento e as alterações cognitivas decorrentes de condições clínicas patológicas. Esta estratégia de **identificação das formas mais ligeiras de declínio** permite potenciar a

precocidade da intervenção clínica junto destes pacientes, um objectivo essencial à obtenção de resultados terapêuticos cada vez mais positivos.

A reconhecida **escassez de instrumentos de avaliação neuropsicológica, particularmente de instrumentos de avaliação cognitiva breve, que tenham sido alvo de um processo rigoroso e sistemático de adaptação, validação clínica e psicométrica e normalização para a população portuguesa**, fundamentou o planeamento inicial do projecto. A perspectiva de poder **contribuir para um diagnóstico mais precoce da demência** e assim melhorar o nível de cuidados de saúde na população portuguesa, reforçou a determinação inicial de concretizar este (ambicioso) programa de investigação.

O início deste projecto coincidiu em termos aproximados com a apresentação do *Montreal Cognitive Assessment* (MoCA; Nasreddine et al., 2005) como um instrumento sensível às formas mais ligeiras de declínio cognitivo. Os excelentes resultados obtidos com esta prova em estudos internacionais, nomeadamente ao nível da sensibilidade ao Défice Cognitivo Ligeiro (DCL), impulsionaram estudos de adaptação e validação em múltiplos países e explicam a sua rápida e ampla difusão a outras situações clínicas para além das originalmente contempladas. O resultado mais evidente desta crescente utilização da prova, e do reconhecimento das suas vantagens sobre outros testes de rastreio cognitivo, foi a sua rápida referenciação em diversas *guidelines* e em estudos de revisão. Neste contexto, a opção pelo MoCA como objecto de estudo do presente projecto decorreu de um modo lógico, impôs-se como a mais adequada e beneficiou parcialmente da experiência acumulada em trabalhos mais circunscritos com a versão experimental portuguesa do MoCA (Martins, 2007; Duro, 2008).

Consideramos que a informação obtida nos sete estudos realizados em Portugal no âmbito da presente tese, bem como os resultados das já numerosas pesquisas publicadas a nível internacional, corroboram a **validade e utilidade clínicas do MoCA**.

Relativamente ao plano de trabalhos inicialmente delineado acrescentámos à validação do MoCA no DCL e DA, a validação clínica da prova à Demência Frontotemporal – variante comportamental (DFTvc) e à Demência Vascular (DV). Com a inclusão destas formas de demência **o programa de trabalhos da presente tese contemplou a grande maioria das causas de deterioração cognitiva do idoso**, criando-se as condições necessárias para a **utilização alargada do MoCA como teste de rastreio cognitivo breve privilegiado no âmbito de consultas de envelhecimento cerebral e demência**.

Deste modo, o plano de trabalhos desenvolvido pretendeu-se sistemático, incluindo sucessivamente estudos de adaptação transcultural, validação psicométrica e clínica e estudos normativos, de forma a proporcionar as **condições necessárias para a utilização rigorosa do MoCA em contexto clínico e em projectos de investigação clínica e epidemiológica a desenvolver na população portuguesa**.

ADAPTAÇÃO TRANSCULTURAL

O processo de adaptação transcultural do MoCA para a população portuguesa constituiu a primeira etapa deste plano de estudos. A utilização de um instrumento numa determinada população sem a conveniente adaptação coloca em risco a validade e precisão dos resultados obtidos. Torna-se, assim, essencial que este processo de adaptação se revista de um rigor metodológico e procedimental que assegure a minimização da influência das diversas fontes de erro inerentes. A procura do máximo de equivalência entre o instrumento original e a versão portuguesa e a preocupação com a validade ecológica da prova na população portuguesa conduziram este longo processo, do qual resultou a **versão final portuguesa do MoCA** e do respectivo **manual de administração e cotação** (Simões, Freitas, Santana, Firmino, Martins, & Nasreddine, 2008).

Este processo de adaptação do MoCA para a nossa população, descrito no **Estudo I** (Freitas, Simões, Martins, Vilar & Santana, 2010), seguiu as orientações metodológicas propostas na literatura (Hambleton & Patsula, 1999; Hambleton, 2005; Herdman, Fox-Rushby, & Badia, 1998; Hill & Hill, 2005; International Test Commission, 2001; Vijver & Poortinga, 2005): tradução, retroversão, realização das correcções necessárias na primeira adaptação linguística do instrumento, contactos com especialistas na área da Psicologia, Neurologia, Psiquiatria e Línguística (com experiência nas áreas da adaptação e validação de testes neuropsicológicos e/ou do envelhecimento), estudos com a primeira versão resultante da adaptação, aplicação do teste a uma amostra representativa das populações alvo, análise das características psicométricas do instrumento na nova população, revisão e novos ajustamentos necessários para finalizar a versão do instrumento, e análise da equivalência entre a versão original e a versão adaptada.

Relativamente a esta última etapa do processo, são muito escassas na literatura as directrizes para a operacionalização da análise de equivalência entre o instrumento original e a versão adaptada. O modelo de avaliação da equivalência da adaptação transcultural de instrumentos de Herdman e colaboradores (1998) é o mais utilizado nos raros estudos de adaptação publicados. De acordo com este modelo, o processo de adaptação do MoCA para a população portuguesa respeitou os diferentes níveis de equivalência apontados pelos autores (equivalência conceptual, de item, semântica, operacional, de mensuração e funcional). Nesta base, e considerando igualmente o envolvimento já referido de especialistas provenientes de diferentes áreas do saber, consideramos que a versão final portuguesa do MoCA apresenta equivalência com a versão original do instrumento, estando por isso convenientemente adaptada para a população portuguesa.

É importante referir que existem diferenças importantes entre a primeira versão experimental (inicialmente utilizada nalguns estudos) e a

versão final portuguesa do MoCA (utilizada nos estudos apresentados neste trabalho), nomeadamente, ao nível dos itens da prova, na lista de palavras incluídas na tarefa de Memória a curto prazo e nas duas frases que contribuem para a avaliação do domínio da Linguagem, para além das diversas alterações efectuadas no manual do MoCA, ao nível das instruções de administração e cotação das tarefas.

Embora constitua um importante parâmetro no processo de validação de um instrumento para uma nova população alvo, a adaptação transcultural e a avaliação da equivalência são apenas o primeiro passo e condição necessária mas não suficiente para a utilização clínica do teste.

VALIDAÇÃO PSICOMÉTRICA

De modo semelhante ao que tem sido globalmente reportado nos estudos internacionais realizados em diversos contextos, as boas propriedades psicométricas do MoCA foram sendo transversal e sistematicamente corroboradas em todos os estudos realizados na população portuguesa, quer com a versão experimental, quer com a versão final da prova. Efectivamente, os estudos descritos neste trabalho, demonstram que o MoCA possui boas qualidades psicométricas quando utilizado na avaliação cognitiva de indivíduos cognitivamente saudáveis e de pacientes com declínio cognitivo.

O *alpha de Cronbach,* enquanto indicador da **consistência interna** da prova, revelou, em todas as amostras estudadas, valores adequados e sistematicamente superiores aos respectivos valores para o MMSE. Os valores de *alpha* variaram entre .648 (*n* = 90 controlos; **Estudo IV**: Freitas, Simões, Alves & Santana, 2012) e .908 (*n* = 102: 34 pacientes com DV, 34 pacientes com DA e 34 controlos; **Estudo VI**: Freitas, Simões, Alves, Vicente & Santana, *submitted*). Estes nossos resultados foram globalmente equiparáveis aos do estudo dos autores da prova, onde foi verificado um *alpha de Cronbach* de .83 numa amostra total heterogénea de 90

participantes controlo, 94 pacientes com MCI e 93 pacientes com DA (Nasreddine et al., 2005), bem como aos dados identificados nos estudos internacionais realizados com o MoCA. Foi ainda possível concluir pela adequação global dos itens uma vez que não se verificou um incremento significativo da consistência interna da prova com a eliminação de qualquer dos seus itens.

Atendendo às características particulares das populações clínicas estudadas, passíveis de manifestar um declínio cognitivo num curto espaço de tempo, a **estabilidade temporal dos resultados** obtidos com o MoCA apenas foi estudada em indivíduos cognitivamente saudáveis. Esta propriedade dos resultados foi analisada numa amostra de 60 controlos, em que 30 tiveram um *follow-up* de 3 meses e outros 30 um *follow-up* de 18 meses, tal como descrito no **Estudo IV** (Freitas, Simões, Alves & Santana, 2012). Em ambos os casos, o MoCA revelou uma excelente estabilidade temporal dos resultados (respectivamente .909 e .877), significativamente mais elevada do que os correspondentes valores para o MMSE (respectivamente .755 e .665). No estudo original de Nasreddine e colaboradores (2005), a estabilidade temporal (.92) foi analisada numa amostra heterogénea (controlos, DCL e DA) de 26 participantes, num intervalo temporal de 35.0 ± 7.6 dias.

O **grau de acordo inter-avaliadores** foi também alvo de análise, tendo-se encontrado excelentes resultados: .988 numa amostra heterogénea (*n* = 60; **Estudo IV**: Freitas, Simões, Alves & Santana, 2012) e .976 numa amostra de 30 pacientes com DFT (**Estudo V**: Freitas, Simões, Alves, Duro & Santana, *submitted*). Na nossa amostra, o menor acordo ocorreu no item correspondente aos *números do desenho do relógio* e nos dois itens de *semelhanças* para a avaliação da capacidade de abstracção. No entanto, a ausência de estudos congéneres não permite a comparação destes resultados. Não obstante, consideramos que a existência do *Manual* com instruções pormenorizadas para a administração e cotação das tarefas

incluídas na prova potencia a estandardização destes procedimentos e, consequentemente, o excelente acordo inter-avaliadores obtido.

Por outro lado, e de um modo geral, os resultados obtidos no MoCA correlacionaram-se positiva e significativamente com os resultados obtidos no MMSE. À semelhança do estudo de Nasreddine e colaboradores (2005) onde foi encontrado um coeficiente de correlação de .87, nos estudos que desenvolvemos os valores correspondentes variaram entre .60 (*n* = 90 participantes controlo; **Estudo IV**: Freitas, Simões, Alves & Santana, 2012) e .85 (*n* = 360: 90 pacientes com DCL, 90 pacientes com DA e 180 controlos; **Estudo IV**: Freitas, Simões, Alves & Santana, 2012), sugerindo a existência de **validade concorrente**.

As correlações positivas e significativas encontradas entre cada item e o respectivo domínio cognitivo (superiores às correlações entre esse item e os demais domínios cognitivos) e entre cada domínio cognitivo e a pontuação total no MoCA (superiores às correlações entre domínios cognitivos) constituem evidências da **validade de constructo** da prova e da capacidade discriminativa dos domínios cognitivos subjacentes. Mesmo assim, e ainda que os diversos estudos realizados apontassem convergentemente para a global fiabilidade e validade psicométrica do MoCA na população portuguesa, foi realizado um estudo mais específico e sistemático para examinar a validade de constructo do MoCA (através do estabelecimento da respectiva validade factorial, convergente e divergente) e da fiabilidade dos resultados obtidos (**Estudo III**: Freitas, Simões, Marôco, Alves & Santana, 2012). Este estudo foi realizado numa amostra de 830 participantes, tendo sido testados diversos modelos com recurso à análise factorial confirmatória: I) um modelo de seis factores conceptualmente proposto pelos autores do MoCA (Nasreddine et al., 2005); II) um modelo de dois factores encontrado por Duro e colaboradores (2010); III) um modelo de factor único de segunda ordem ("Cognição")]. Ainda que todos os modelos testados revelassem bons índices de ajustamento, o modelo de seis factores conceptualmente proposto pelos autores da prova (Nasreddine

et al., 2005) revelou um ajustamento significativamente melhor. Os nossos resultados permitiram ainda o estabelecimento da validade factorial, convergente e divergente desta estrutura de seis factores e, deste modo, da respectiva validade de constructo. Adicionalmente a análise dos itens revelou uma boa adequação psicométrica e foram ainda encontradas sólidos indicadores de fiabilidade dos resultados. Concluindo, estes dados constituem evidências sucessivas de que o MoCA para além de constituir uma válida e fiável medida da capacidade cognitiva global do indivíduo, possibilita legitimamente a **análise de perfis cognitivos** com base nas (seis) dimensões subjacentes, facilitando aos clínicos e investigadores uma interpretação mais compreensiva das aptidões cognitivas com base numa avaliação cognitiva breve.

VALIDAÇÃO CLÍNICA

Reconhecendo a importância de uma investigação científica alicerçada nas necessidades clínicas reais e tendo como objectivo o exame da **aplicabilidade clínica do MoCA no âmbito das consultas dirigidas à população com declínio cognitivo e demência**, equacionámos adicionalmente a realização de três estudos de validação clínica. No primeiro estudo foi analisada a **precisão diagnóstica e estabelecidos os pontos de corte óptimos para o Declínio Cognitivo Ligeiro (DCL) e a Doença de Alzheimer (DA)** (**Estudo IV**: Freitas, Simões, Alves & Santana, 2012), no segundo estudo trabalhámos os mesmos objectivos para a **Demência Fronto-Temporal-variante comportamental (DFTvc)** (**Estudo V**: Freitas, Simões, Alves, Duro & Santana, *submitted*) e, num terceiro, para a **Demência Vascular (DV)** (**Estudo VI**: Freitas, Simões, Alves, Vicente & Santana, *submitted*). Nestes estudos, todos os grupos controlo foram emparelhados quanto ao género, idade e escolaridade com os pacientes dos grupos clínicos. Adicionalmente, os grupos clínicos de cada estudo foram equiparados, para além do género, idade e escolaridade, quanto ao

nível de severidade do declínio cognitivo, de acordo com a pontuação no MMSE.

De um modo consistente e transversal a estas três investigações, o MoCA evidenciou melhor capacidade discriminante e precisão diagnóstica do que o MMSE na diferenciação entre os grupos clínicos e os respectivos grupos controlo constituídos por indivíduos cognitivamente saudáveis residentes na comunidade. Como esperado, os participantes cognitivamente saudáveis dos grupos controlo obtiveram melhores desempenhos do que qualquer um dos grupos clínicos considerados. Os resultados evidenciaram ainda diferenças estatisticamente significativas em todos os domínios cognitivos entre todos os grupos clínicos e os respectivos grupos controlos. Por outro lado, os pacientes com DCL obtiveram melhores pontuações totais e melhores desempenhos em todos os domínios cognitivos do MoCA do que os pacientes com DA (**Estudo IV**: Freitas, Simões, Alves & Santana, 2012). Quanto à análise comparativa dos desempenhos dos pacientes com diferentes tipos de demência, apesar de previamente equiparados quanto ao nível de severidade de acordo com a pontuação no MMSE, foram observadas diferenças estatisticamente significativas na pontuação total obtida no MoCA, com pior desempenho para os pacientes com DA comparativamente aos pacientes com DFTvc. Estes resultados sugerem uma efectiva diferença na capacidade discriminativa do MoCA e do MMSE. Adicionalmente, os pacientes com DA revelaram um perfil cognitivo com pior desempenho no domínio da memória e no domínio visuoespacial quando comparados com os pacientes com DFT (**Estudo V**: Freitas, Simões, Alves, Duro & Santana, *submitted*). No entanto, ainda que estes estudos de validação clínica apontem para uma significativa potencialidade do MoCA na diferenciação do perfil cognitivo dos pacientes, nomeadamente no que diz respeito aos domínios cognitivos avaliados, os resultados não foram tão promissores na comparação entre pacientes com DV e pacientes com DA. Neste estudo, não foram encontradas diferenças estatisticamente significativas nem na pontuação total no MoCA, nem quanto aos domínios

cognitivos examinados (**Estudo VI**: Freitas, Simões, Alves, Vicente & Santana, *submitted*). Atendendo aos resultados obtidos nos outros dois estudos de validação clínica, consideramos que esta indiferenciação de desempenhos entre pacientes com DV e pacientes com DA poderá reflectir um perfil cognitivo mais próximo entre estas condições clínicas, quando equiparado o nível de severidade, mais do que uma insuficiência do instrumento para diferenciar desempenhos. Uma futura replicação deste estudo com uma amostra mais alargada poderá elucidar melhor esta questão.

Relativamente aos pontos de corte óptimos, à semelhança de outras investigações internacionais (Damian et al., 2011; Lee et al., 2008; Luis, et al., 2009; Zhao et al., 2011), os nossos estudos apontam valores inferiores aos 26 pontos, propostos pelos autores da prova como pontuação de corte para o défice cognitivo (Nasreddine et al., 2005) e frequentemente citados e utilizados em outros estudos publicados, sem averiguação da sua adequação às populações. Consideramos que as diferenças a este nível são, em grande medida, justificadas pela discrepância na escolaridade média entre as populações alvo. Com efeito, as nossas amostras mostraram de um modo sistemático um nível médio de escolaridade significativamente inferior ao do estudo conduzido por Nasreddine e colaboradores (2005). Para além disso, atendendo à capacidade do MoCA em distinguir diferentes níveis de severidade do declínio cognitivo, optámos por estabelecer pontos de corte distintos para a população com DCL e com demência. Esta abordagem é, no nosso entender, mais útil, rigorosa e informativa do que o estabelecimento de um ponto de corte único, como proposto noutros estudos similares, nomeadamente no trabalho original de Nasreddine e colaboradores (2005).

Assim, com um ponto de corte óptimo de 22 pontos para o DCL, o MoCA apresentou bons valores de sensibilidade, especificidade, valor preditivo positivo, valor preditivo negativo e de precisão classificatória. Estes indicadores foram significativamente superiores aos respectivos valores

encontrados para o MMSE, que evidenciou uma pobre precisão diagnóstica na identificação dos indivíduos com DCL. Estes resultados confirmam a inadequação do uso do MMSE para o rastreio breve das formas mais ligeiras de défice cognitivo, dada a elevada probabilidade de falsos negativos. Esta é uma questão relevante uma vez que todas as orientações recentes reforçam a importância de uma identificação precoce do declínio cognitivo e paradoxalmente, continua a observar-se o uso generalizado do MMSE, apesar das suas limitações serem frequentemente referenciadas na literatura.

Relativamente à demência, os três estudos de validação clínica (**Estudo IV**: Freitas, Simões, Alves & Santana, 2012; **Estudo V**: Freitas, Simões, Alves, Duro & Santana, *submitted*; **Estudo VI**: Freitas, Simões, Alves, Vicente & Santana, *submitted*), permitiram definir o ponto de corte de 17 pontos como óptimo para a identificação da DA, DFTvc e DV, estando a este associados excelentes valores de sensibilidade, especificidade, valor preditivo positivo, valor preditivo negativo e de precisão classificatória. Estes resultados, quando comparados com os respectivos valores encontrados para o MMSE, corroboram a superioridade discriminativa e precisão diagnóstica do MoCA.

Recentemente, nos NINDS-CSN VCI Harmonization Standards criteria (Hachinski et al., 2006) é proposta uma versão abreviada do MoCA como um *protocolo de 5 minutos* para o rastreio cognitivo de pacientes com défices cognitivos vasculares. Os nossos resultados indicam que esta versão abreviada apresenta uma capacidade discriminativa entre os pacientes com VD e os indivíduos cognitivamente saudáveis equiparável à versão completa original do MoCA. Com um ponto de corte óptimo de 8 pontos, este *protocolo de 5 minutos* demonstra uma excelente precisão diagnóstica, com elevados valores de sensibilidade, especificidade, valor preditivo positivo, valor preditivo negativo e de precisão classificatória, não tendo sido encontradas diferenças estatisticamente significativas em comparação com o MoCA versão completa. Estes resultados validam a

versão abreviada para a avaliação cognitiva breve em pacientes com DV, permitindo uma economia de tempo que poderá ser muito útil em contexto clínico (**Estudo VI**: Freitas, Simões, Alves, Vicente & Santana, *submitted*).

Por fim, os dados preliminares do estudo longitudinal com pacientes com DCL e DA (**Estudo IV**: Freitas, Simões, Alves & Santana, 2012) corroboram a excelente sensibilidade do MoCA ao declínio cognitivo num reduzido intervalo de tempo [176.81 ± 67.09 dias; min.= 63; max.= 340] em ambos os grupos clínicos, em oposição aos resultados com o MMSE que se revelaram insensíveis ao declínio cognitivo longitudinal nos pacientes com DCL. Nesta análise longitudinal, verificou-se que os pacientes com DCL apenas apresentavam deterioração do desempenho ao nível da capacidade de memória, enquanto os pacientes com DA revelaram decréscimo dos desempenhos no domínio da atenção, concentração e memória de trabalho, e no domínio da orientação temporal e espacial. Deste modo, e para além da utilidade confirmada ao nível do rastreio cognitivo breve e da quantificação do declínio cognitivo, o MoCA parece ser também um instrumento útil na **monitorização da evolução clínica dos pacientes**, quer em termos quantitativos quer qualitativos (padrões de evolução cognitiva). Esta capacidade para além de grande interesse para a prática clínica, poderá justificar a pertinência da selecção deste instrumento para investigações que visem a **avaliação de intervenções terapêuticas em pacientes com declínio cognitivo**, nomeadamente ao nível dos ensaios clínicos.

NORMAS E INFLUÊNCIA DE VARIÁVEIS NO DESEMPENHO

Ainda que diversos estudos internacionais tenham vindo a reportar a influência de diversas variáveis sociodemográficas e de saúde no desempenho em testes de rastreio cognitivo, até ao momento não existem estudos publicados que abordem essa influência no MoCA. Uma das tarefas do nosso projecto foi a concretização desse objectivo. Deste modo, e com

recurso a uma amostra da comunidade cognitivamente saudável, estratificada de acordo com as principais variáveis sociodemográficas e representativa da população portuguesa, analisamos a influência das variáveis sociodemográficas (idade, escolaridade, género, estado civil, situação profissional, região geográfica, localização geográfica e área de residência) e de saúde (história familiar de demência, sintomatologia depressiva e queixas subjectivas de memória) nos desempenhos no MoCA (**Estudo II**: Freitas, Simões, Alves & Santana, 2012).

De acordo com a maioria dos estudos previamente publicados (Anderson et al., 2007; Bravo & Hébert, 1997; Gallacher et al., 1999; Langa et al., 2009; Matallana et al., 2011; Mathuranath et al., 2007; Moraes et al., 2010), os nossos resultados confirmam que **idade e escolaridade** constituem as variáveis sociodemográficas que mais significativamente contribuem para a predição da pontuação total no MoCA, explicando 49% da variância total dos resultados, sendo que idades mais avançadas e níveis de escolaridade mais baixos aumentam a probabilidade de piores desempenhos.

Dados relativos à influência de outras variáveis sociodemográficas em testes de rastreio cognitivo breve não reúnem o mesmo consenso na literatura. No nosso estudo, o género, o estado civil e a situação profissional não revelaram um efeito significativo sobre os resultados no MoCA. Quanto às variáveis de carácter mais geográfico, a localização geográfica (litoral/interior) e a área de residência não revelaram uma influência significativa, tendo o efeito da região geográfica sido reduzido e provavelmente modelado pelas diferenças verificadas ao nível da idade e escolaridade.

No que respeita à influência das variáveis de saúde no desempenho no MoCA (**Estudo II**: Freitas, Simões, Alves & Santana, 2012), os nossos resultados sugerem, à semelhança do estudo de Mías e colaboradores (2007), que não existe uma associação significativa entre a (in)existência de história familiar de demência e o desempenho em testes cognitivos breves

em indivíduos cognitivamente saudáveis. Outra variável contemplada, o nível de queixas subjectivas de memória, foi duplamente operacionalizada: considerando a percepção do participante e de acordo com a avaliação por um informador próximo. As queixas de memória tal como avaliadas por um informador próximo não se correlacionaram significativamente com os resultados no MoCA obtidos por indivíduos cognitivamente saudáveis. No entanto, as queixas subjectivas de memória percepcionadas pelo próprio participante e o nível de sintomatologia depressiva em indivíduos sem diagnóstico de Depressão apresentaram uma correlação significativa e negativa com a pontuação obtida no MoCA. Contudo, atendendo aos resultados da regressão linear múltipla realizada, apenas as queixas subjectivas de memória avaliadas pelo próprio participante demonstraram uma reduzida contribuição (9%) para a explicação da variância dos resultados no MoCA.

A análise da influência de diversas variáveis no desempenho no MoCA, permitiu não só reunir informação complementar importante para uma avaliação mais objectiva e compreensiva do desempenho cognitivo individual, como também constituiu um passo fundamental para a selecção dos critérios mais adequados para o estabelecimento dos dados normativos para a população portuguesa. Tendo-se comprovado a forte influência da idade e da escolaridade no desempenho no MoCA, estas variáveis emergiram como os critérios óptimos para o estabelecimento dos dados normativos do MoCA para a população portuguesa (**Estudo VII**: Freitas, Simões, Alves & Santana, 2011). Estes resultados vão ao encontro da tendência verificada na literatura, na medida em que a magnitude do efeito **da idade e escolaridade** sobre o desempenho em testes cognitivos é tão forte que invariavelmente estas variáveis são utilizadas como **critério para a definição de dados normativos** (cf., Bravo & Hébert, 1997; Guerreiro, 1998; Han et al., 2008; Mathuranath et al., 2007; Measso et al., 1993; Morgado et al., 2009).

PONTOS FORTES E LIMITAÇÕES

Definimos como objectivo geral do presente plano de trabalhos proporcionar as condições fundamentais para a utilização adequada do MoCA em contexto clínico e de investigação na população portuguesa. Pretendíamos assim colmatar uma importante lacuna na área da **avaliação neuropsicológica em Portugal**, promovendo e potenciando a utilização do MoCA, nomeadamente no âmbito das consultas de declínio cognitivo e de demência. De um modo geral pensamos ter alcançado esse objectivo, cumprindo um **programa de investigação** simultaneamente sistemático e ambicioso.

Nessa trajectória de investigação, o **estudo normativo** constituía uma das tarefas mais exigentes. Concretizámo-la, estudando uma amostra representativa da população portuguesa, estratificada de acordo com as principais variáveis sociodemográficas, e com uma distribuição real muito próxima da distribuição da população portuguesa.

Relativamente aos **estudos de validação clínica** parece-nos importante salientar que foram desenvolvidos num centro de excelência do nosso país (Serviço de Neurologia dos Hospitais da Universidade de Coimbra), com acesso a meios de diagnóstico sofisticados, o que permite assegurar uma elevada acuidade de diagnóstico. Por outro lado, na análise dos resultados foram considerados grupos controlo emparelhados quanto ao género, idade e escolaridade com os diversos grupos clínicos estudados, sendo que os grupos clínicos entre si também foram emparelhados quanto aos mesmos critérios e, adicionalmente, quanto à pontuação no MMSE (com vista a aproximar os grupos quanto ao nível de severidade), seguindo-se rigorosamente esta metodologia em todos os estudos realizados.

O **tamanho das amostras** foi igualmente alvo de atenção, procurando-se o seu incremento e, deste modo, assegurar uma maior representatividade, sem prejuízo para o rigor dos critérios de inclusão e exclusão adoptados e estritamente cumpridos. Neste sentido, os participantes cognitivamente saudáveis que não cumpriam integralmente

todos os critérios para inclusão no estudo e os pacientes sem diagnóstico bem estabelecido, em situação clínica de significativa comorbilidade ou com elevada severidade dos défices cognitivos, foram sempre excluídos dos estudos.

A **homogeneidade dos grupos clínicos investigados** com o MoCA constitui uma vantagem adicional dos estudos apresentados. Em amostras clínicas heterogéneas, as análises e subsequentes conclusões extraídas podem facilmente ser enviesadas. Ainda que tenha tido implicações ao nível do tamanho (mais reduzido) dos grupos clínicos, optámos por incluir apenas o subtipo amnésico (domínio único ou múltiplos domínios) no grupo de pacientes com DCL, a variante comportamental no grupo de pacientes com DFT, e pacientes com DV 'pura'. A homogeneidade foi ainda extensível à equivalência no tamanho dos grupos intra-estudo, reduzindo assim possíveis enviesamentos resultantes de diferentes tamanhos dos grupos nas análises estatísticas.

Por fim, importa ainda salientar a **reduzida variabilidade inter-avaliador** dos resultados apresentados. Uma vez que todos os participantes cognitivamente saudáveis foram avaliados por apenas duas psicólogas com experiência em avaliação neuropsicológica e que os pacientes foram maioritariamente avaliados por uma destas psicólogas, foi possível maximizar a estandardização dos procedimentos inerentes ao processo de avaliação.

Contudo, os vários estudos que compõem este trabalho apresentam algumas **limitações** que não podíamos deixar de identificar.

A primeira limitação, ainda que derive de uma premissa conceptual inerente ao instrumento, é a **exclusão dos indivíduos iletrados**. Para além da comprovada influência da escolaridade no desempenho no MoCA, alguns dos seus itens são objectivamente inadequados para avaliar indivíduos analfabetos. A administração da prova a estes sujeitos conduziria a que alguns itens fossem sistematicamente pontuados com zero e, nessa

medida, a um significativo “efeito chão” com implicações ao nível da sensibilidade do teste ao défice cognitivo. A avaliação dos indivíduos iletrados requer uma significativa adaptação das tarefas a este contexto ou, idealmente, instrumentos especificamente desenvolvidos para este fim.

De registar também que na amostra de indivíduos cognitivamente saudáveis, o **subgrupo mais jovem** apresenta uma **escolaridade média significativamente superior ao subgrupo mais idoso**, dificultando assim a tarefa de equiparar todas as faixas etárias consideradas na estratificação quanto ao nível de escolaridade. Esta dificuldade reflecte o perfil demográfico real do nosso país, onde apenas nas últimas décadas se instituiu o aumento da escolaridade mínima obrigatória ao nível secundário. Esta medida tem já um impacto no aumento da escolaridade média da camada mais jovem, continuando, contudo, a população idosa portuguesa a caracterizar-se por um nível de escolaridade substantivamente muito baixo.

Outra limitação que pode ser apontada é a **classificação e operacionalização dos participantes da comunidade “como cognitivamente saudáveis”**, sem acesso a avaliação clínica e/ou meios complementares de diagnóstico, e exclusivamente com base na colheita de informações e de avaliação neuropsicológica. Mesmo assim, é de salientar que procurámos utilizar **critérios de inclusão e exclusão exigentes** (corroborados com base em diferentes dados na entrevista clínica e na avaliação neuropsicológica realizadas) que assegurassem, dentro do possível, a "normalidade" do estado cognitivo dos participantes. Adicionalmente, para os participantes com idades mais avançadas procuramos obter informação confirmatória junto dos respectivos clínicos gerais e/ou de outros informadores próximos. Reconhecemos que uma consulta de neurologia e a disponibilidade e facilidade de acesso a exames diagnósticos complementares teriam constituído importantes contributos. Contudo, o tamanho da amostra, a distribuição geográfica desta e o próprio âmbito de financiamento deste projecto impossibilitaram essa implementação.

No que respeita à **análise da influência das variáveis de saúde** no desempenho no MoCA, nomeadamente quanto à sintomatologia depressiva e às queixas subjectivas de memória, consideramos que os resultados devem ser interpretados com cautela (exclusivamente para indivíduos cognitivamente saudáveis sem diagnóstico de Depressão) e que esta análise **carece de melhor operacionalização** num estudo futuro. A inclusão de instrumentos de avaliação mais compreensivos e de grupos clínicos com psicopatologia, nomeadamente com diagnóstico de Depressão, permitirá uma análise mais precisa e completa da influência destas variáveis no desempenho em provas cognitivas como o MoCA.

Quanto aos **estudos de validação clínica**, o critério de homogeneidade adoptado, que nos parece fundamental para o rigor das conclusões extraídas, introduz algumas **restrições à generalização dos seus resultados**. Referimos a título de exemplo o estudo de validação para o DCL, no qual apenas foram incluídos pacientes com DCL subtipo amnésico, pelo que a generalização dos resultados para o DCL em geral deve ser cautelosa. A mesma crítica pode ser apontada à impossibilidade de generalização dos resultados obtidos com o grupo clínico de DFTvc para as demais variantes da DFT.

Ainda que os resultados da análise preliminar do **estudo longitudinal com pacientes com DCL e DA** sejam promissores, esta investigação requer continuidade e **necessidade de mais momentos de avaliação e de amostras mais robustas**.

Por fim, como referido ao longo dos diversos estudos realizados, a inexistência de estudos nacionais ou internacionais similares impossibilitou a comparação de alguns dos nossos resultados, nomeadamente, no **Estudo II**, referente à influência das variáveis sociodemográficas e de saúde no desempenho no MoCA (Freitas, Simões, Alves & Santana, 2012); no **Estudo III,** onde foi efectuada a validação de constructo da prova (validação factorial, convergente e discriminante) (Freitas, Simões, Marôco, Alves & Santana, 2012); na análise do acordo inter-avaliadores descrita no

Estudo IV (Freitas, Simões, Alves & Santana, 2012); no **Estudo V**, de validação clínica do MoCA para pacientes com a variante comportamental da DFT (Freitas, Simões, Alves, Duro & Santana, *submitted*); no **Estudo VI**, de validação clínica do MoCA para pacientes com DV [escala completa e versão abreviada proposta pelos NINDS-CSN VCI Harmonization Standards criteria (Hachinski et al., 2006) (Freitas, Simões, Alves, Vicente & Santana, *submitted*)]; e no **Estudo VII**, onde foram estabelecidos dados normativos com base numa amostra estratificada e representativa (Freitas, Simões, Alves & Santana, 2011).

ESTUDOS FUTUROS

Porque a investigação centrada na validação de um instrumento de avaliação é sempre um projecto inacabado que requer continuidade e porque os estudos realizados proporcionaram respostas mas felizmente geram sempre novas questões, o programa de trabalhos de validação dos resultados no MoCA para a população portuguesa não se esgota nestas páginas nem se encerra com o fechar deste ciclo.

Neste sentido, diversos estudos estão planeados, e alguns destes estão já em fase de avançada de execução, nomeadamente: I) Continuidade do estudo longitudinal com pacientes com DCL e DA; II) Continuidade da avaliação com grupos específicos de psicopatologia; III) Estudo de adaptação e validação das duas versões alternativas do MoCA para a população portuguesa; IV) Estudo de correlação do MoCA com biomarcadores no DCL e na DA; V) Estudos no âmbito da validade concorrente, nomeadamente com o Teste do Desenho do Relógio, a *Alzheimer's Disease Assessment Scale* (ADAS), o *Addenbrooke's Cognitive Examination* (ACE-R) e com a Escala de Inteligência de Wechsler para Adultos (WAIS-III); e VI) Análise dos itens com recurso à Teoria de Resposta ao Item (TRI).

CONCLUSÃO

O MoCA é um instrumento de avaliação cognitiva breve útil, eficaz e com elevada difusão internacional. Com a conclusão do plano de estudos desenvolvido e apresentado nesta dissertação, podemos referir que o **MoCA se encontra adaptado, validado clínica e psicometricamente, e dispõe de normas representativas para a população portuguesa**. Estão assim criadas as condições necessárias para a sua utilização em contexto clínico e de investigação, no nosso país.

Os estudos de natureza psicométrica asseguram a validade do instrumento na população portuguesa, evidenciam as **boas qualidades psicométricas das pontuações** obtidas com a prova e fundamentam a possibilidade de utilizar a avaliação dos domínios cognitivos do MoCA para o **estabelecimento de perfis cognitivos**.

Os estudos de validação clínica comprovam a **capacidade discriminativa e a elevada precisão diagnóstica dos resultados**, legitimando a sua utilização em tarefas de rastreio cognitivo breve. Estão assim criadas as condições para que o MoCA possa ser utilizado em contextos de saúde menos especializados, nomeadamente nos cuidados primários de saúde. Por outro lado, o leque de patologias mais específicas estudadas permite que a utilização do MoCA seja igualmente implementada em consultas especializadas de declínio cognitivo e demência. A análise longitudinal revelou ainda uma **excelente sensibilidade do MoCA ao declínio cognitivo ao longo do tempo**, ampliando a sua utilização ao controlo da evolução e monitorização dos efeitos terapêuticos.

O estudo normativo permitiu a **elaboração de normas para a população portuguesa** essenciais para uma análise e interpretação comparativa dos desempenhos. Os resultados aqui apresentados fundamentam a elegibilidade do MoCA para futuros estudos epidemiológicos e populacionais no nosso país.

Deste modo, consideramos que foi alcançado o objectivo global a que nos propusemos: disponibilizar um instrumento que constitui uma

excelente opção para a avaliação cognitiva breve. Com este trabalho pensamos ter contribuído para o desenvolvimento da avaliação neuropsicológica em Portugal e para uma melhoria dos cuidados de saúde, possibilitando uma identificação precoce do declínio cognitivo na nossa população.

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ANEXO I

Montreal Cognitive Assessment

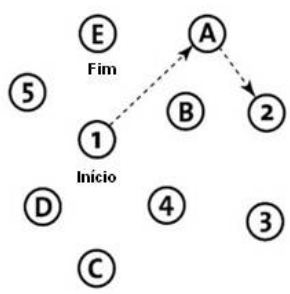
Versão Portuguesa do Teste

MONTREAL COGNITIVE ASSESSMENT (MOCA)

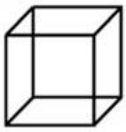
VERSÃO PORTUGUESA

Nome: _____ Idade: _____
Género: _____ Data de Nascimento: _____
Escolaridade: _____ Data de Avaliação: _____

VISUO-ESPACIAL / EXECUTIVA — Pontos



Copiar o cubo



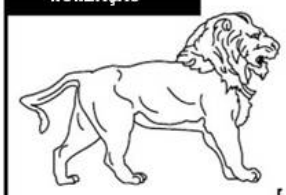
[ ] [ ]

Desenhar um Relógio (onze e dez) (3 pontos)

[ ] Contorno [ ] Números [ ] Ponteiros

__/5

NOMEAÇÃO



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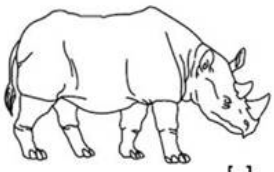
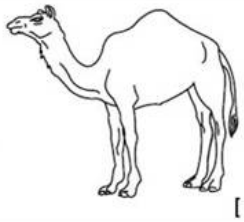


[ ]



[ ]

__/3

MEMÓRIA — Leia a lista de palavras. O sujeito deve repeti-la. Realize dois ensaios. Solicite a evocação da lista **5 minutos mais tarde**.

	Boca	Linho	Igreja	Cravo	Azul
1º ensaio					
2º ensaio					

Sem Pontuação

ATENÇÃO — Leia a sequência de números. (1 número/segundo) — O sujeito deve repetir a sequência. [ ] 2 1 8 5 4 — O sujeito deve repetir a sequência na ordem inversa. [ ] 7 4 2 — __/2

Leia a série de letras (1 letra/segundo). O sujeito deve bater com a mão cada vez que for dita a letra A. Não se atribuem pontos se ≥ 2 erros.
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B — __/1

Subtrair de 7 em 7 começando em 100. [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 ou 5 subtracções correctas: 3 pontos; 2 ou 3 correctas: 2 pontos; 1 correcta: 1 ponto; 0 correctas: 0 pontos — __/3

LINGUAGEM — Repetir: Eu só sei que hoje devemos ajudar o João. [ ] O gato esconde-se sempre que os cães entram na sala. [ ] — __/2

Fluência verbal: Dizer o maior número possível de palavras que comecem pela letra "P" (1 minuto). [ ] ____ (N ≥ 11 Palavras) — __/1

ABSTRACÇÃO — Semelhança p.ex. entre banana e laranja = fruta [ ] comboio - bicicleta [ ] relógio - régua — __/2

EVOCAÇÃO DIFERIDA — Deve recordar as palavras SEM PISTAS

	Boca	Linho	Igreja	Cravo	Azul
	[ ]	[ ]	[ ]	[ ]	[ ]
Opcional Pista de categoria					
Opcional Pista de escolha múltipla					

Pontuação apenas para evocação SEM PISTAS — __/5

ORIENTAÇÃO — [ ] Dia do mês [ ] Mês [ ] Ano [ ] Dia da semana [ ] Lugar [ ] Localidade — __/6

© Z.Nasreddine MD

Examinador: _____

TOTAL __/30

Versão Portuguesa: M.R. Simões, S. Freitas, I. Santana, H. Firmino, C. Martins, Z. Nasreddine & M. Vilar 2008 – Serviço de Avaliação Psicológica, FPCE-UC & HUC

ANEXO II

Montreal Cognitive Assessment

Versão Portuguesa do Manual

MONTREAL COGNITIVE ASSESSMENT (MoCA)

MANUAL DE ADMINISTRAÇÃO E COTAÇÃO

Mário R. Simões
Sandra Freitas
Isabel Santana
Horácio Firmino
Cristina Martins
Ziad Nasreddine
Manuela Vilar

2008

Faculdade de Psicologia e Ciências da Educação

da Universidade de Coimbra & Hospitais da Universidade de Coimbra

MONTREAL COGNITIVE ASSESSMENT (MoCA)

Instruções para a Administração e Cotação

O *Montreal Cognitive Assessment* (MoCA) foi concebido como um instrumento de rastreio breve da disfunção cognitiva ligeira. Este instrumento avalia diferentes domínios cognitivos: função executiva; capacidade visuo-espacial; memória; atenção, concentração e memória de trabalho; linguagem; e orientação temporal e espacial. O tempo de administração é de aproximadamente 10 a 15 minutos. A pontuação máxima é de 30 (pontos).

1. Alternância Conceptual *(Trail MakingTest* B - adaptado)

Administração: Assinalando o espaço adequado na folha de protocolo, o examinador apresenta, de forma pausada, as seguintes instruções ao sujeito: ***"Neste espaço existem alguns números e letras. Gostaria que desenhasse uma linha, sem levantar a caneta, alternando entre números e letras, respeitando a ordem dos números e do alfabeto. Comece aqui no número 1*** (apontar para o número 1) ***e desenhe uma linha até à letra A, continue até ao número 2, e depois continue para a letra seguinte e por aí adiante alternando entre números e letras, até chegar à letra E. Termine aí*** (apontar a letra E)**"**. No caso de o sujeito não ter compreendido as instruções, estas devem ser repetidas integralmente. Durante a execução da tarefa, não devem ser fornecidas quaisquer ajudas.

Cotação: Atribuir 1 ponto se o sujeito desenha com sucesso a seguinte sequência (sem desenhar qualquer linha cruzada): 1-A-2-B-3-C-4-D-5-E.

Atribuir 0 pontos se a sequência não é respeitada ou se, durante a execução, o sujeito não corrigir imediatamente um erro, qualquer que ele seja.

2. Capacidades Visuo-Espaciais (Cubo)

Administração: O examinador apresenta as seguintes instruções, apontando para o cubo: ***"Copie este desenho do modo mais parecido que conseguir, no espaço em baixo. Avise quando terminar."***. Não devem ser fornecidas quaisquer ajudas ou indicações adicionais ao sujeito.

Cotação: Atribuir 1 ponto se a figura for desenhada correctamente:

- O desenho deve ser tridimensional e na mesma perspectiva;
- Estão presentes (desenhadas) todas as linhas;
- Não são acrescentadas linhas;
- As linhas são relativamente paralelas e aproximadamente do mesmo comprimento (são aceitáveis prismas rectangulares).

Atribuir 0 pontos se não forem respeitados todos os critérios anteriormente assinalados.

3. Capacidades Visuo-Espaciais (Relógio)

Administração: Assinalando o espaço adequado, o examinador apresenta as seguintes instruções: ***"Agora gostaria que desenhasse um relógio redondo. Coloque todos os***

números no relógio e, no final, marque 11 horas e 10. Quando terminar avise. Percebeu?". Repetir as instruções se o sujeito não compreender. Uma vez iniciada a tarefa, não devem ser fornecidas ajudas ou orientações ao sujeito. Não deve ser feita referência aos "ponteiros".

Cotação: Atribuir 1 ponto por cada um dos três critérios seguintes:

- **Contorno** (1 pt.): O contorno deve ser um círculo pouco deformado (p. ex., é permitida uma leve deformação de fechamento do círculo).
- **Números** (1 pt.): Todos os números devem estar presentes, sem números adicionais. Os números têm de estar na ordem correcta e colocados de forma adequada, nos quadrantes do mostrador do relógio. São aceitáveis números romanos, bem como a colocação dos números fora do contorno do círculo (no exterior do círculo).
- **Ponteiros** (1 pt.): Os dois ponteiros devem indicar a hora correcta. O ponteiro das horas deve ser claramente mais pequeno que o ponteiro dos minutos. O ponto de junção dos ponteiros deve estar colocado aproximadamente no centro do relógio.

Atribuir 0 pontos por cada critério anterior não respeitado.

4. Nomeação

Administração: Começando da esquerda para a direita, na perspectiva do sujeito, o examinador pede ao sujeito para dizer o nome de cada um dos animais: ***"Diga-me o nome deste animal."*** (apontar para o leão). ***"E deste?"*** (apontar para o rinoceronte). ***"E deste?"*** (apontar o camelo/dromedário).

Cotação: Atribuir 1 ponto por cada nomeação correcta: (1) leão; (2) rinoceronte; (3) camelo ou dromedário.
Atribuir 0 pontos por cada nomeação incorrecta.

5. Memória

Administração: O examinador lê uma lista de 5 palavras, ao ritmo de uma palavra por segundo, logo após ter apresentado as seguintes instruções: **"*Isto é um teste de memória. Eu vou ler uma lista de palavras que deve memorizar. Escute com atenção! Quando eu terminar, vou pedir-lhe que diga todas as palavras de que se consegue lembrar. Pode dizê-las pela ordem que quiser. Está preparado(a)? "Boca, Linho, Igreja, Cravo, Azul*".**

O examinador lê a lista de palavras uma primeira vez e regista a ordem (1º, 2º, 3º, 4º, 5º), no espaço reservado para esse efeito, pela qual o sujeito consegue repetir/evocar as palavras.

Quando o sujeito tiver terminado (lembrou-se de todas as palavras ou quando não conseguir lembrar-se de mais palavras), o examinador volta a ler a lista de palavras após as seguintes instruções: "***Agora vou ler novamente a mesma lista de palavras. No final, tente recordar-se e dizer-me o maior número de palavras que conseguir, incluindo as palavras que repetiu da primeira vez. Está preparado(a)? "Boca, Linho, Igreja, Cravo, Azul*".**

No espaço reservado para o efeito, o examinador regista a ordem (1º, 2º, 3º, 4º, 5º) pela qual o sujeito repetiu as palavras no segundo ensaio.

No final do segundo ensaio, o examinador informa o sujeito que deverá memorizar a lista de palavras e que

terá de voltar a repeti-las, mais tarde: **"*Peço-lhe que memorize estas palavras. Irei pedir que as repita, de novo, mais tarde*".**

Cotação: Não é atribuída pontuação à prova de memória (evocação imediata, ensaios 1 e 2).

6. <u>Atenção</u>

6.1 <u>Sequência numérica em sentido directo</u>

Administração: O examinador lê uma sequência de 5 dígitos, ao ritmo de um dígito por segundo, logo após ter dado as seguintes instruções: **"*Vou dizer-lhe alguns números. Quando acabar, quero que repita esses números pela mesma ordem que eu os disse. Está preparado(a)? Atenção! 2-1-8-5-4*".**

6.2 <u>Sequência numérica em sentido inverso</u>

Administração: O examinador lê uma sequência de 3 dígitos, ao ritmo de um dígito por segundo, logo após ter dado as seguintes instruções: **"*Agora vou dizer-lhe mais alguns números. Quando acabar, quero que repita esses números na ordem inversa à que lhe disse, diga-os ao contrário. Por exemplo, se eu lhe disser 1-3, deve dizer-me 3-1. Está preparado(a)? Atenção! 7-4-2*".**

Cotação: Atribuir 1 ponto por cada sequência repetida correctamente (a ordem exacta de repetição da sequência numérica em sentido inverso é 2-4-7).

Atribuir 0 pontos, por cada repetição incorrecta (sentido directo e sentido inverso).

6.3 Concentração (Cancelamento)

Administração: O examinador lê uma série de letras, ao ritmo de uma letra por segundo, logo após ter dado as seguintes instruções: **"*Vou ler várias letras. Sempre que eu disser a letra A, bata com a mão na mesa. Quando eu disser uma outra letra diferente, não bata com a mão. Está preparado(a)?*".**

Cotação: Atribuir 1 ponto se a execução é correcta (admite apenas a ocorrência de um erro).

Atribuir 0 pontos se houver mais de um erro, isto é, ≥ 2 erros (considera-se erro quando o sujeito bate com a mão sendo a letra dita errada – outra letra que não A; ou quando o sujeito não bate com a mão, tendo sido dita a letra A).

6.4 Subtracção em série de 7

Administração: O examinador apresenta as seguintes instruções: "***Agora vou pedir-lhe que me diga quanto é 100 menos 7 e, depois, continue a tirar 7 ao número que deu como resposta. Vá retirando sempre 7, até eu lhe dizer para parar. Percebeu? Está preparado(a)?*".** Repetir a instrução duas vezes, se necessário, antes do início da realização da tarefa. Parar, após serem efectuadas 5 subtracções (independentemente de estarem ou não correctas).

Cotação: Nesta prova, a pontuação máxima possível é de 3 (pontos). A pontuação será de 0 pontos se nenhuma subtracção estiver correcta. Atribuir 1 ponto por uma subtracção correcta; 2 pontos por duas ou três subtracções correctas; e 3 pontos por quatro ou cinco subtracções correctas.

Cada subtracção é avaliada individualmente, isto é, se o sujeito comete um erro de subtracção, mas depois faz subtracções de 7 correctas, a partir do número que dá como resposta, é atribuída pontuação a essas respostas. Por exemplo, um sujeito responde 100-7= 92-85-78-71-64; a resposta "92" é incorrecta, mas os números seguintes foram correctamente subtraídos, pelo que se deve atribuir uma pontuação de 3 (pontos).

No caso de o sujeito recorrer à estratégia de contar pelos dedos, não deve haver penalização, uma vez que esta estratégia é compensatória, implicando a utilização de recursos disponíveis e não prejudicando a Atenção, Concentração e Memória de Trabalho que a tarefa pretende avaliar.

Se o sujeito não efectuar subtracções sucessivas de modo espontâneo, deve ser dito apenas: "***Continue, até eu lhe pedir para parar.***".

No caso de o sujeito não recordar o número resultante da última subtracção, deve dar-se a indicação "***Procure lembrar-se …***". Se ele ainda assim, não conseguir recordar, então dizer o último número mas penalizar a subtracção imediatamente seguinte (cotar como zero). Do mesmo modo deve ser penalizada a subtracção a partir de um número distinto do resultado referido. O resultado das subtracções seguintes segue o procedimento de cotação geral previsto para a tarefa.

7. Repetição de frases

Administração: O examinador dá as seguintes instruções: "***Agora vou ler uma frase. Quero que a repita, tal como eu a disser, com as mesmas palavras, logo depois de eu terminar de a ler*** [pausa]:

"***Eu só sei que hoje devemos ajudar o João***".

Após esta primeira tarefa, o examinador diz:

"***Agora vou ler outra frase. Quero que a repita, tal como eu a disser, com as mesmas palavras, logo depois de eu terminar de a ler*"** [pausa]:

"***O gato esconde-se sempre que os cães entram na sala***".

Cotação: Atribuir 1 ponto por cada frase repetida correctamente. A repetição deve ser exacta. O examinador deve prestar atenção aos erros por omissão (p. ex., omitir "hoje" ou "só"), substituição (p. ex., trocar "devemos" por "havemos"; "o gato" por "os gatos"; "que" por "quando") e/ou adição (p. ex., "na sala de jantar").

Atribuir 0 pontos, por cada frase repetida incorrectamente.

8. Fluência Verbal Fonémica

Administração: O examinador apresenta as seguintes instruções: **"*Agora vou pedir-lhe que diga o maior número possível de palavras que comecem por uma determinada letra, que lhe vou dizer a seguir. Pode dizer qualquer tipo de palavra, menos nomes próprios, como nomes de pessoas ou de lugares. Por exemplo, se eu disser "A", o(a) senhor(a) pode dizer "água" ou "andar", mas não pode dizer "António" ou "Aveiro". Também não pode***

usar duas ou mais palavras da mesma família (p. ex. galinha, galinheiro). Percebeu? [Caso o sujeito não tenha entendido voltar a dar as instruções]. ***Tem um minuto para dizer o maior número de palavras que se lembrar, que comecem pela letra P, como por exemplo, pai.*** [Tempo: 60 segundos]. ***Pare!***"

Cotação: Atribuir 1 ponto se o sujeito disser 11 ou mais palavras em 60 segundos. Registar as respostas do sujeito no verso da folha de protocolo.

Atribuir 0 pontos se o sujeito disser menos de 11 palavras (< 11 palavras).

9. <u>Abstracção (Semelhanças)</u>

Administração: O examinador pede ao sujeito que diga o que têm em comum dois elementos apresentados, ilustrando com o seguinte exemplo: **"*Diga-me agora em que são parecidas uma banana e uma laranja?*".** Se o sujeito dá uma resposta concreta (p. ex., têm casca), o examinador repete apenas mais uma vez: "***Diga-me em que mais são parecidas uma banana e uma laranja?***". Se o sujeito não dá uma resposta adequada (são frutos/fruta), o examinador deve dizer: **"*Sim, e ambas são frutos*"**. Não dar quaisquer outras instruções ou explicações.

Depois do ensaio (item de treino), o examinador diz: **"*Agora diga-me, em que são parecidos um comboio e uma bicicleta?*"**.

Após a resposta do sujeito, o examinador deve perguntar: **"*E em que são parecidos um relógio e uma régua?***".

Não dar pistas ou instruções suplementares.

Cotação: Apenas os dois últimos itens são cotados (o item de treino não é cotado). Atribuir 1 ponto por cada resposta correcta (pontuação máxima possível: 2 pontos).

- São **aceitáveis** as seguintes respostas:

– *comboio / bicicleta*: p. ex.: meios de transporte, veículos, meios de locomoção, para viajar, servem para as pessoas se deslocarem, servem para levar as pessoas ao seu destino.

– *régua / relógio*: p. ex.: instrumentos de medição, para medir, para marcar (tempo e distâncias), têm escala.

- Respostas **não aceitáveis**:

– *comboio / bicicleta*: p. ex.: andam, têm rodas, têm banco, têm condutor, são feitos de metal, levam pessoas, etc.

– *régua / relógio*: p. ex.: têm números, servem para bater (régua serve para bater na mão, na escola, e relógio bate as horas), são espalmados, são rectangulares, começam pela letra "r", etc.

10. Evocação Diferida

Administração: O examinador dá as seguintes instruções: "***Li há pouco uma lista de palavras, que depois o(a) senhor(a) repetiu, por duas vezes. Pedi-lhe que a memorizasse para repetir mais tarde. Agora, diga todas as palavras que conseguir recordar***". O examinador assinala pela ordem de evocação (1, 2, 3, 4, 5), no espaço para esse efeito, todas as palavras que o sujeito evoca sem a ajuda de pistas.

Nota importante: A evocação diferida deve ocorrer após 5 minutos da aprendizagem da lista, mesmo que isso implique alterar a ordem de administração dos itens.

Cotação: Atribuir 1 ponto por cada uma das palavras recordadas sem qualquer pista.

Opcional:

Para as palavras que o sujeito não recorda espontaneamente, o examinador proporciona pistas de categoria semântica. Em seguida, para as palavras que o sujeito não recorda, mesmo com pistas de categoria semântica, o examinador oferece uma selecção de respostas possíveis e o sujeito deve identificar a palavra adequada (reconhecimento). Apresentamos, no quadro que se segue, as pistas para cada palavra:

Palavra	Pista de categoria	Escolha múltipla
Boca	parte do corpo	nariz, boca, mão
Linho	tipo de tecido	lã, algodão, linho
Igreja	tipo de edifício	igreja, escola, hospital
Cravo	tipo de flor	rosa, cravo, tulipa
Azul	uma cor	azul, vermelho, verde

Cotação: não se atribuem pontos às palavras recordadas com pistas. Assinalar com um *visto* (√), no espaço para esse efeito, as palavras que foram ditas a partir de uma pista (de categoria semântica ou de escolha múltipla). Ao serem proporcionadas pistas, os dados obtidos nesta prova oferecem informação clínica sobre a natureza das dificuldades mnésicas. Quando se trata de dificuldades de recuperação de informação, o desempenho pode melhorar graças às pistas. No caso de dificuldades no processo de codificação, as pistas não melhoram o desempenho.

11. Orientação

Administração: O examinador dá as seguintes instruções: **"*Diga-me qual é a data de hoje?*"**. Se o sujeito der uma resposta incompleta, o examinador diz; **"*Diga o ano, o mês, o dia***

***do mês (data) e o dia da semana*"** (não questionar para as categorias temporais que o sujeito já referiu). A seguir, o examinador pergunta: **"*Diga como se chama o lugar onde estamos agora e em que cidade/vila/aldeia nos encontramos*".**

Cotação: Atribuir 1 ponto por cada item correctamente respondido. O sujeito deve saber a data exacta e o local exacto (hospital, clínica, consultório, etc.).
Atribuir 0 pontos por cada resposta incorrecta.

Pontuação Total

Some todos os pontos assinalados na margem direita da folha de protocolo (para uma pontuação máxima possível de 30 pontos).

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