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Research paper

Lifetime affective problems and later-life cognitive state: Over 50 years of follow-up in a British birth cohort study

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ABSTRACT

Background: Affective problems increase the risk of dementia and cognitive impairment, yet the life course dimension of this association is not clearly understood. We aimed to investigate how affective problems across the life course relate to later-life cognitive state.

Methods: Data from 1269 participants from the Medical Research Council National Survey of Health and Development (NSHD, the British 1946 birth cohort) were used. Prospectively-assessed measures of affective symptoms spanning ages 13–69 and categorised into case-level thresholds. Outcomes consisted of a comprehensive measure of cognitive state (Addenbrooke's Cognitive Examination (ACE-III)), verbal memory, and letter search speed and accuracy at age 69.

Results: Complementary life course models demonstrated that having 2 or more case-level problems across the life course was most strongly associated with poorer cognitive outcomes, before and after adjusting for sex, childhood cognition, childhood and midlife occupational position and education.

Limitations: A disproportionate loss to follow-up of those who had lower childhood cognitive scores may have led to underestimation of the strength of associations.

Discussion: Using a population-based prospective study we provide evidence that recurrent lifetime affective problems predicts poorer later-life cognitive state, and this risk can be already manifest in early old age (age 69). Our findings raise the possibility that effective management to minimise affective problems reoccurring across the life course may reduce the associated risk of cognitive impairment and decline.

1. Introduction

Many studies have demonstrated an association between depression and anxiety – affective symptoms – and subsequent cognitive impairment and dementia (Cherbuin et al., 2015; da Silva et al., 2013; Gulpers et al., 2016; John et al., 2018; Jorm, 2001; Ownby et al., 2006; Stella et al., 2014). The severity, frequency and onset of symptoms are thought to be important features in establishing the nature of these associations (Bennett and Thomas, 2014; Byers and Yaffe, 2011; da Silva et al., 2013; Kaup et al., 2016; Köhler et al., 2010; Richards et al., 2014; Singh-Manoux et al., 2017), and feasibly affect cognitive function before dementia onset (Brailean et al., 2008; Butters et al., 2008; Luppa et al., 2013), perhaps through hippocampal atrophy (MacQueen and Frodl, 2011; McKinnon et al., 2009); although findings for cognitive decline are more inconsistent (Brailean et al., 2017). However, few studies have had long-term follow-up of affective symptoms and thus little is known about the life course accumulation of affective symptoms, and the relevance of symptom timing, in relation to later-life cognitive state (Richards et al., 2014; Riddle et al., 2017).

Using the Medical Research Council (MRC) National Survey of Health and Development (NSHD) – the British 1946 birth cohort – no clear pattern of association between longitudinal profiles of affective symptom trajectories derived from latent class analysis (aged 13–53 years) and level and change in cognitive test scores at ages 53 and 60–64 was found, even after adjusting for childhood cognitive ability, education and midlife socioeconomic position (Richards et al., 2014). However, participants may have still been relatively young; the symptom profiles did not allow the investigation of timing effects; and

Abbreviations: ACE-III, Addenbrooke's Cognitive Examination third edition; CI, confidence interval; GHQ-28, 28-item General Health Questionnaire; MRC, Medical Research Council; NSHD, National Survey of Health and Development

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the cognitive outcomes may not have sufficiently captured aspects of function relevant to dementia risk (Richards et al., 2014). A new wave of cognitive data has now been collected on participants at age 69, repeating the cognitive function tests used previously, and adding one of the most detailed measure of cognitive state, the Addenbrooke's Cognitive Examination third edition (ACE-III) (Hsieh et al., 2013). Using complementary life course models can help to test the cumulative and temporal effects of affective symptoms on later-life cognitive state.

The aim of the present study was to investigate the cumulative association between case-level affective problems measured from adolescence to later-life and later life cognitive function at age 69, after accounting for sex, childhood cognition, educational attainment and lifetime socioeconomic position. We further aimed to investigate temporal effects of symptom occurrence by examining the incidence of affective problems in later life compared with earlier life, testing whether cumulative or time period life course models best described the data. We hypothesised that having more case-level affective problems across the life course would be associated with lower cognitive function in older age, independently of these potential confounders.

2. Methods

2.1. Participants

The NSHD is a representative sample of 5362 males and females who were born in England, Scotland and Wales in one week in March 1946 (Wadsworth et al., 2006). The 24th data collection was conducted between 2014 and 2015 when participants were aged 68–69 years (Kuh et al., 2016). At age 69, following a postal questionnaire at age 68, participants still alive and with a known current address in mainland Britain ($n = 2698$) were invited to have a home visit; 2149 (79%) completed a visit (see Supplementary Fig. I for a flow diagram of the sample). For this data collection, we obtained ethical approval from the NRES Queen Square REC (14/LO/1073) and Scotland A REC (14/SS/1009). All participants gave written informed consent to collect these data. Research was conducted in accordance with the Helsinki Declaration.

2.2. Cognitive outcomes

The ACE-III, a test of cognitive state (Hsieh et al., 2013), was used as the primary outcome measure. The ACE-III is divided into five domains: attention and orientation (scored 0–18); verbal fluency (0–14); memory (0–26); language (0–26); and visuospatial function (0–16). Thus the maximum total score is 100. A customised version of the ACE-III was administered by iPad using ACEMobile (http://www.acemobile.org); where this was not possible, a paper version was used. All offline scoring was undertaken by trained personnel. Of the 2149 participants with a home visit at age 69, 32 refused or were unable to undertake the ACE-III at all. Of the remaining 2117, 35 attempted but did not fully complete due to equipment error and inability to complete all sections and data from 353 participants were corrupt through equipment failure such as exporting data and the fieldwork agency being unable to retrieve the data from the iPad. Thus complete ACE-III data were available for 1729 participants, 81% of those who received home visit.

Of the 2149 participants with a home visit, 2102 (98%) completed a short-term verbal memory test and a processing speed test previously given at ages 43, 53 (Richards et al., 2004) and 60–64 years (Richards et al., 2014). The verbal memory test consisted of a 15-item word learning task devised by the NSHD. Similar to previous analyses (Richards et al., 2014), the total number of words correctly recalled over three identical trials was summed to provide an overall score for short-term verbal memory (maximum 45). Processing speed was assessed by a visual search task, where participants were required to cross out the letters P and W, randomly embedded within a page of other letters, as quickly and accurately as possible within 1 min. Letter search speed was represented by the position reached at the end of this interval (maximum 600) and letter search accuracy was represented by the number of target letters correctly crossed out within this interval (maximum 84). The degree of cognitive decline in the cohort using these measures has previously been described (Davis et al., 2017).

2.3. Lifetime affective symptoms measures

Due to the nature of data collection across the entire lifespan, different assessments of affective symptoms were necessary at specific ages. In order to use the most clinically meaningful metric at each age we identified those with a level of symptom severity consistent with a possible clinical diagnosis of affective disorder, referenced as those with “case-level symptoms”. More detailed information about the measures and validation of cut-off thresholds to indicate case-level symptoms can be found in Supplementary Table I. Briefly, at ages 13 and 15 years teacher ratings of behaviour and temperament were obtained using a forerunner of the Rutter A scale (Rutter, 1967). Factor scores at ages 13 and 15 years were summed to create scales representing a dimension of emotional problems, and were standardised to a mean of 0 and SD of 1. Frequency and severity of common symptoms of depression and anxiety were also assessed in adulthood, with the short community version of the Present State Examination at 36 years (Wing et al., 1974), the Psychiatric Symptom Frequency scale at 43 years (Lindelow et al., 1997), and the 28-item General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979) at ages 53, 60–64, and 69 years. In line with previous studies (Hatch et al., 2009), for each total score thresholds for case-level symptoms were imposed, representing potentially diagnosable common mental disorder. For the adolescent teacher ratings this was the 91st to 100th percentile (Colman et al., 2007). For the Present State Examination this was the standard Index of Definition ≥ 5. For the Psychiatric Symptom Frequency scale this was greater than 22 (Lindelow et al., 1997) which has been shown to capture service contact for common mental disorders, relevant medication prescription and suicidal ideation. The threshold for the GHQ-28 was the recommended 4/5 cut for summed scores each recoded from the Likert scale to the binary scale (Goldberg and Hillier, 1979). The number of times participants met case threshold across testing waves were summed and recoded as follows: (a) never case-level ($n = 764$); (b) once only ($n = 464$); (c) twice or more ($n = 313$). Case level frequencies are shown in Supplementary Table II.

To investigate effects of later incidence (age 60+) of case-level affective problems compared to earlier incidence (<age 60), a variable was generated with four levels: (a) never case-level ($n = 764$); (b) No case-level incidence aged 60+ but previously case-level ($n = 401$); (c) case-level incidence aged 60+ and previously case-level ($n = 220$); (d) first incidence of case-level aged 60+ ($n = 156$) (Fig. 1).

2.4. Covariates

Consistent with previous analyses (Richards et al., 2014) the following variables were treated as potential confounders in additional models: sex, childhood occupational position, childhood cognitive ability (Hatch et al., 2007; Richards et al., 2001), adult occupational position and educational attainment (Opdebeeck et al., 2016; Richards et al., 2014); to investigate whether associations were those with fluid cognitive functions, and to further reduce the possibility of reverse causality, a measure of general cognitive ability, the National Adult Reading Test, was additionally adjusted (Nelson, 1991; Richards and Sackers, 2003) (Fig. 1).

Childhood cognitive function at age 8 was represented as the sum of four tests of verbal and non-verbal ability devised by the National Foundation for Educational Research (Pigeon, 1964). Childhood occupational position was derived from paternal occupation; adult occupational position was derived from participants' own occupation at 53 years, given that this is when most people are expected to be in work, or