in England and Wales (Gunnell et al., 2003; Lodhi and Shah, 2004), Sweden (Carlsten et al., 1999) and Australia (Hall et al., 2003). There may be several reasons for this. First, the sample size was small. Second, some countries may use older antidepressants for which data on the AI were absent. Third, the AI does not take into account awareness of depression among individuals and their carers, identification of depression by healthcare professionals, appropriateness of treatment for depression offered by healthcare professionals, and compliance for taking antidepressants by patients. Fourth, the AI does not take account of different payment systems for prescriptions: in some countries healthcare professionals may dispense medication directly without charging the patient; in countries with welfare systems elderly patients may be exempt from paying directly for their prescription; and, in other countries, prescription costs may be covered by insurance. Fifth, treatments such as cognitive behavior therapy may be offered in some countries instead of antidepressants. If the AI for all antidepressants can be calculated for all the countries where the patient has to pay for the antidepressant prescription at the time of presenting the prescription then the true relationship between elderly suicide rates and the AI of antidepressants can be examined.

Apathy is a syndrome of executive dysfunction that exists in patients with late-life depression

Marin et al. (2003) have suggested that apathy may be independent of executive functions in older-aged patients with major depression, although the correlation between apathy and the “controlled oral word association test,” a test of executive measures, approached significance. However, Feil et al. (2003), using the same definition and measure of apathy, observed a strong correlation between apathy and both verbal and non-verbal executive cognitive measures. The question thus arises as to whether apathy contributes to executive cognitive dysfunction in non-demented patients with late-life depression. We therefore re-examined this issue, looking particularly at whether apathy distinctly affects executive control functions. Our hypothesis was that apathy would contribute to cognitive impairment in depressed elderly patients independently of the severity of depression.

In our prospective cohort study, we enrolled 84 patients from the geriatric psychiatric clinic of the Chang Gung Memorial Hospital with major depressive disorder. The inclusion criteria included a diagnosis of unipolar major depression based on DSM-IV. The exclusion criteria included a diagnosis of dementia of the Alzheimer’s type or vascular dementia based on the DSM-IV criteria. Patients with a history of any psychiatric disorders other than major depression, or neurological disorders that may influence cognition, were also excluded. All participants were administered the 17-item Hamilton rating scale for depression (Ham-D) to evaluate their depression status. Among these Ham-D items, the apathy-related items included diminished work/interest, anergy, lack of insight, and psychomotor retardation. These items showed a robust correlation with the Apathy Evaluation Scale (Marin et al., 1991) and ranged in score from 0 to 12. We therefore used the apathy-related items of the Ham-D as a proxy measure of apathy.

We employed pairs of behavioral tasks to assess whether apathy has a distinct effect on executive control functions. Each pair of tests consisted of an executive and a non-executive task. First, we assessed verbal fluency as an executive cognitive measure with object naming as a non-executive control function. Second, we examined backward digit span as an executive cognitive measure with

References


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the forward digit span as a non-executive control function. Finally, we assessed orientation to time and orientation to personal information and place as a pair of executive and non-executive tasks.

The demographic and clinical data of the study participants are presented in Table S1 (available online attached to the electronic version of this letter at www.journals.cambridge.org/jid_IPG). The mean age was 67.7 (± 6.3 SD) years and mean education level 5.8 (± 4.4 SD) years of education. The mean score of the 17-item Ham-D was 12.5 (± 4.9 SD) with a mean apathy score of 3.2 (± 1.5 SD).

For each outcome measure obtained from the neuropsychological tests, we performed a linear regression with apathy score, non-apathy Ham-D score, the interaction between the two tests, age and years of education as regressors. We included the interaction between the apathy and non-apathy score in order to assess the interactional effect of apathy and depression on cognitive performance. Age and years of education were included as “nuisance” covariates. Table S2 (available online attached to the electronic version of this letter at http://www.journals.cambridge.org/jid_IPG) summarizes the results of the regression analyses. For each test pair, apathy – but not depression or the interaction between apathy and depression – significantly contributed to the executive task performance. Depression only accounted for the significant difference in the performance of digit forward span, a short-term memory task.

This study shows that apathy accounts for most of the performance variance in orientation to time, verbal fluency, and backward digit span, which is consistent with our hypothesis that apathy plays a major role in moderating cognitive executive dysfunction in patients with late-life depression. Neither apathy nor the interaction between apathy and depression predicted the non-executive task of the test pair. However, even if depression predicts one non-executive task in this study, the result does not solidly conclude that late-life depressed patients are vulnerable in non-executive functions, which would require verification through a direct comparison between our patients and healthy participants. The current results provide further evidence that apathy is a motivational/cognitive syndrome distinct from depression. Given that frontal-subcortical pathway and executive dysfunction are associated with late-life depression (Marin et al., 2003), apathy appears to compromise the fronto-striatal network that mediates cognitive executive functions. Cognitive executive functions comprise complex thinking abilities, mental flexibility/set shifting, and goal-directedness. Deficits in executive function are associated with impairment in activities instrumental to daily living (Kiosses et al., 2000).

The finding of apathy may deserve particular attention in the treatment and care of patients with late-life depression.

To improve studies of apathy, depression and executive function in late-life depression, we suggest the following: (1) Further studies with a longitudinal design are necessary to examine the reliability of these associations. (2) The four apathy items of the Ham-D examined a limited range of symptoms and signs; further studies employing a fully validated apathy scale such as the Apathy Evaluation Scale would provide a more reliable measure of apathy (Marin et al., 1991). (3) Because mild cognitive impairment (MCI) could potentially account for the association between apathy and cognitive impairment in older participants, further studies should rule out the possibility of MCI. On the other hand, our results suggest that apathy is specifically associated with impairment in executive functions and not with a general decline in cognitive capacity. (4) The inclusion of healthy control individuals will provide a means of assessing directly the effect of apathy and depression on cognitive and affective functions in patients with major depression.

In conclusion, the current findings indicate that apathy is a syndrome of executive dysfunction that exists in patients with late-life depression. Apathy is associated with executive dysfunction, which increases the risk of functional impairments. Because of this, identifying apathy could contribute to the care of the elderly, particularly those with major depression.

References


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