CASE REPORT

Effect of non-pharmacological intervention for apathy: response to one-on-one reminiscence-based intervention

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SUMMARY

Apathy has adverse consequences for patients and caregivers. However, the therapeutic approach remains uncertain. Here, we present the case of a man aged 67 years who only developed apathy after surgery for oesophageal cancer. He showed no response to intervention with donepezil, a 'brain training' video game and psychoeducation for apathy. Subsequently, we implemented a programme designed to facilitate recall of 2 themes (editorial content and television shows during the week) once a week. After 3 months, the scores of 2 apathy scales rated by the patient's wife, psychological test scores and brain perfusion single-photon emission CT data improved compared with those obtained before intervention. These results may be attributable to activated 2-way communication as well as benefits of reminiscence therapy, as seen in patients with dementia. Further studies are needed to develop additional non-pharmacological interventions that activate 2-way communication for apathetic patients in ways appropriate to their interests and comorbidities.

BACKGROUND

Apathy, as defined by Levy and Dubois,¹ is an observable behavioural syndrome consisting of a quantitative reduction in voluntary or goal-directed behaviour, and is often encountered in neurodegenerative diseases such as dementia. Patients with apathy do not report about a change, but apathy symptoms cause great concern to their family or caregivers and over time seriously impact the patients' quality of life and well-being.^{2 3}

However, there is currently no established effective therapy for apathy.⁴⁻⁶ We present a case of apathy in which there was no response to intervention with donepezil, a 'brain training' video game and psychoeducation for apathy; however, one-on-one reminiscence-based intervention was effective. We believe that the findings in this case provide useful clues regarding intervention for apathy.

CASE PRESENTATION

A man aged 67 years with no history of smoking, alcohol consumption or oral medication was informed of a lump in the neck detected on MRI at a routine check-up and was diagnosed as having oesophageal cancer in our surgery unit. He underwent curative surgical resection for an oesophageal tumour but declined preoperative and postoperative chemotherapy or radiotherapy. Histopathologically, the tumour was a moderately differentiated

squamous cell carcinoma, finally diagnosed as stage IIb (T1bN1M0) according to the American Joint Committee on Cancer staging manual.⁷ After surgery, he developed pneumonia and remained in hospital for 1 month. During this period, he developed symptoms of apathy which continued for 6 months until his wife brought him to our outpatient department. He had worked as a civil servant until retirement at 60 years of age and had been in good health until the diagnosis of oesophageal cancer. He had an amiable personality and had no history of mental disorder and no family history of mental disorder.

At the initial visit, he answered the questions with no feeling and did not symptom about any changes. He had no symptoms of depressed mood, guilt, suicidal ideation, sleep disorders or loss of appetite in the Japanese version of the GRID-Hamilton Depression Scale-21 (total score=9). The Wechsler Adult Intelligence Scale, Third Edition (WAIS-III) score did not show cognitive decline (table 1). He had no neurological abnormalities such as tremor, muscular rigidity or indistinct speech. Brain MRI showed no evidence of organic disease such as pituitary tumour or metastatic tumour (figure 1). Whole-body fluorodeoxyglucose-positron emission tomography and follow-up examinations including squamous cell carcinoma antigen (1.3 ng/mL; normal: 0–1.5 ng/mL), cytokeratin-19 fragments (2.5 ng/mL; normal: 0–3.5 ng/mL), assessment of other laboratory data, gastrointestinal fibroscopy and CT scans showed no evidence of recurrence following surgery.

However, the Apathy Evaluation Scale Informant Version (AES-I)⁸ score and the Neuropsychiatric Inventory (NPI) apathy score rated by his wife showed apathy (table 1). Also, brain perfusion single-photon emission CT (SPECT) demonstrated distinct hypoperfusion in the frontal lobes bilaterally, especially in the prefrontal areas, which might be associated with the neuroanatomical basis of apathy (figure 2).^{9 10} Based on these results, we diagnosed the patient as having apathy without comorbidity.

First, he was treated with donepezil (an acetyl cholinesterase inhibitor) after being provided with full explanations and information regarding the drug, including the off-label use. Next, he was asked to play a 'brain training' video game that he had often played a few years earlier, for a minimum of 10 min every day for 2 months from 3 months after the start of pharmacotherapy.

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Table 1 Results of Wechsler Adult Intelligence Scale-Third Edition (WAIS-III), Apathy Evaluation Scale Clinician Version (AES-C) and Apathy score of Neuropsychiatric Inventory (NPI)

	Before intervention*	After intervention*
WAIS-III		
Full IQ(FIQ)	106	117
Verbal IQ (VIQ)	110	118
Performance IQ (PIQ)	101	112
AES-C†	62	45
Apathy score of NPI		
Frequency‡	4 very often	2 sometimes
Severity§	3 severe	1 mild
Distress¶	4 severely	2 mildly

*Intervention: one-on-one reminiscence-based intervention.

†AES-C: cut-off score of Japanese version=45/46.⁸

‡Frequency: very often—nearly always present; sometimes—about once per week.

§Severity: severe—apathy is very evident and usually fails to respond to any encouragement or external events, mild—apathy is notable but produces little interference with daily routine; only mildly different from patient's usual behaviour; patient responds to suggestions to engage in activities.

¶Distress: severely—disruptive, upsetting to staff and other residents, major time infringement, mildly—almost no change in work routine but little time rebudgeting required.

During these periods, he and his wife returned for follow-up visits once every 2 weeks and received psychoeducational intervention for apathy. However, he showed no visible sign of recovery. His wife declined to switch to another off-label medication for apathy, and she also reported about having to prompt him to play the video game every day. These interventions were therefore discontinued.

Subsequently, we encountered the findings of a controlled clinical trial for apathy in patients with dementia conducted by Politis *et al*⁶ in which one-on-one reminiscence-based intervention and one-on-one intervention without reminiscence were effective. Thus, we designed a similar programme for a patient without dementia which we then used for our patient. The aim was to facilitate recall of week-long daily activities before each hospital visit for half an hour once a week with the guidance of a psychologist in order to activate two-way communication. Reminiscence consisted mainly of the following two themes. One was newspaper editorial content. He was asked to read editorials every day and talk about them at each session, because he had a habit of reading the newspaper. Second was television (TV) shows. He was asked to talk about favourite or interesting TV shows which he had watched during the week, because he spent most of his time in front of the TV screen. The sessions were held for 3 months.

After this intervention, the apathy score and caregiver distress score in AES-I and NPI rated by his wife had decreased compared with values obtained before intervention; his IQ scores were

higher than before intervention (table 1). Furthermore, brain perfusion SPECT revealed increased perfusion in the frontal lobes bilaterally compared with before the intervention (figure 2).

INVESTIGATIONS

The following four tests were performed before and after non-pharmacological intervention.

The NPI apathy score and AES-I score rated by his wife suggested an improvement in apathy (table 1).

In the WAIS-III, scores for the arithmetic, picture arrangement, picture completion and block design subtests were 7, 2, 4 and 2 points higher than those before intervention, respectively. The increase in his IQ scores was attributed to these results. Other subtests were about the same level as the previous tests (table 1).

SPECT images were obtained using a double-head rotating gamma camera (SymbaTM E; Toshiba Medical System, Tokyo, Japan) equipped with a parallel collimator, ~15 min after intravenous injection of 111 MBq of N-isopropyl-*p*-[¹²³I] iodoamphetamine (IMP). SPECT images were analysed using a 3D stereotactic surface projections (3D-SSP) programme, iSSP 5 V1.0 (Nihon Medi-Physics Co., Tokyo, Japan) that was incorporated into the FALCON software package. Data were quantified and displayed by the use of the stereotactic extraction estimation (SEE) programme, SEE V2.1 (Nihon Medi-Physics Co.).¹¹ IMP distribution of the cortex on 3D-SSP was compared with normal database (27 normal controls). Differences between individual data and normal database in each pixel were converted to the Z score calculated using the following formula: Z score = ((control mean) – (individual value)) / (control SD). The cluster of pixels with significant difference (Z score > 1.96) could be identified as the target area with a reduced blood flow on Z score maps (figure 2). Extent ratio (%) of pixels with significant reduction within a target was calculated as follows: extent ratio (%) = pixel count value of Z score ≥ 1.96 / total pixel count value. The mean Z score and extent ratio in both frontal lobes before and after the non-pharmacological intervention were as follows: before the intervention; mean Z score (SD) left = 3.51 (1.23), right = 3.51 (1.30), extent ratio left = 44.7% and right = 43.8%, after the intervention; mean Z score left = 3.20 (0.94), right = 2.87 (0.80), extent ratio left = 19.5% and right = 20.8%.

DIFFERENTIAL DIAGNOSIS

Depression should be included in the differential diagnosis of apathy. Differentiating between apathy and depression is often difficult because of the overlap in clinical features, such as diminished interest, pleasure or activity.¹² In the present case, symptoms which were helpful in making the diagnosis of apathy including absence of emotional distress, depressed mood, guilt, suicidal ideation, sleep disorders and appetite disorders.

Figure 1 Axial and sagittal T1-weighted MRI scans of the brain.

Figure 2 Three-dimensional stereotactic surface projections of statistical Z scores representing area of functional reduction in the patient: (A) before one-on-one reminiscence-based intervention, (B) after one-on-one reminiscence-based intervention. RT. LAT, right lateral view; LT. LAT, left lateral view; SUP, superior view; INF, inferior view; ANT, anterior view; POST, posterior view; RT. MED, right middle view; LT. MED, left middle view. A positive Z score represents a reduced regional cerebral blood flow relative to the control mean. The Z score in each Z map image is scaled from 1.96 to 7.

TREATMENT

First, donepezil was given in a daily dose of 5 or 10 mg for 5 months. Next, intervention using the brain training video game was added during the final 2 months of pharmacotherapy. During these periods, he and his wife returned for follow-up visits once every 2 weeks and received psychoeducational intervention for apathy. However, he showed no visible sign of recovery. Therefore, these interventions were discontinued. Subsequently, one-on-one reminiscence-based intervention was continued for 3 months and had a useful role in improving apathy.

OUTCOME AND FOLLOW-UP

Three months after completing the last session, the patient showed sustained improvement of apathetic symptoms. He is scheduled to return for follow-up visits once a month.

DISCUSSION

We tried four types of therapeutic interventions for this patient diagnosed with apathy without comorbidity.

Regarding pharmacological treatment, donepezil alone was ineffective in this case. Treatment of apathy in patients with

dementia and Parkinson's disease with acetylcholinesterase inhibitors, dopaminergic drugs and psychostimulants has been reported with some clinical benefits.⁴ However, no randomised and well-controlled studies have confirmed these observations.^{4, 5} Therefore, the effectiveness of pharmacological treatment for apathy may be limited at the present time.

Intervention using the brain training video game raised the patient's score for some tasks but was ineffective for apathy. This finding supported the conclusion drawn by Owen *et al*¹³ that computer-based brain training confers no greater benefit than simply answering general knowledge questions. This type of intervention could be of little benefit to apathetic patients.

Psychoeducational intervention was also ineffective for apathy in this case. One-way communication in which the patient talks less may not have any beneficial effect on apathy.

Conversely, as shown in the results of the four tests, one-on-one reminiscence-based intervention was effective for apathy.

The NPI apathy score and the AES-I score which were based on the observation of the patient's wife matched the changes in her mental state elicited by apathy. That is, she grew irritable

and showed no expression before the intervention but showed a soft expression on her face after the intervention. This finding suggests the credibility of the two apathy scales.

In the WAIS-III test, arithmetic, picture arrangement, picture completion and block design subtests which were associated with the increase in his IQ scores were assessed under a time limit. Therefore, in these tasks, the patient could give more correct answers within the time limit after the intervention than before intervention. These results suggest the improvement of decreased psychomotor speed which is thought to be a feature of apathy.

Longitudinal brain perfusion SPECT imaging data in this case showed improvement of hypoperfusion in the frontal lobes bilaterally. Given that imaging studies have shown that apathy in Alzheimer's disease is associated with hypoperfusion in regions that are involved in frontal-subcortical networks,^{9 10} this finding suggests a possible beneficial effect of one-on-one reminiscence-based intervention.

Generally, reminiscence is a psychosocial intervention that is commonly used in the elderly and in dementia treatment. The primary goal is to facilitate recall of past experiences in order to become more involved with others. Themes, props and triggers, such as photographs, and archive sound recordings are also used to achieve the goals of reminiscence therapy.⁶ Reminiscence is divided into individual and group types. Sessions are usually held once a week for 30–60 min and one course lasts a few months. But there is no structured routine.

In the current case, the goal of one-on-one reminiscence-based intervention was to facilitate recall in order to activate two-way communication and to ultimately improve apathy. To achieve this goal, we established two everyday themes that were

familiar to the patient. And these themes were week-long daily activities before each hospital visit to make it easier to recall, because he did not have dementia. The results suggested that apathy may be improved by activating two-way communication with a psychologist by way of recall of two themes. Moreover, based on the findings of Politis *et al*⁶ mentioned earlier, reminiscence and other methods may be useful to activate two-way communication in patients with apathy.

Further studies are needed to develop additional non-pharmacological interventions that activate two-way communication of patients with apathy in ways appropriate to their interests and comorbidities.

Contributors AO identified and managed the case, and is the guarantor of the paper. TU was responsible for the programme of one-on-one reminiscence-based intervention and the assessment of psychological tests.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- Longitudinal brain perfusion single-photon emission CT data may be useful for assessing the effectiveness of treatment for apathy.
- Non-pharmacological interventions that activate two-way communication of apathetic patients by means of reminiscence or other methods may be effective for apathy.
- Further studies are needed to develop additional non-pharmacological interventions that activate two-way communication of apathetic patients in ways appropriate to their interests and comorbidities.

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