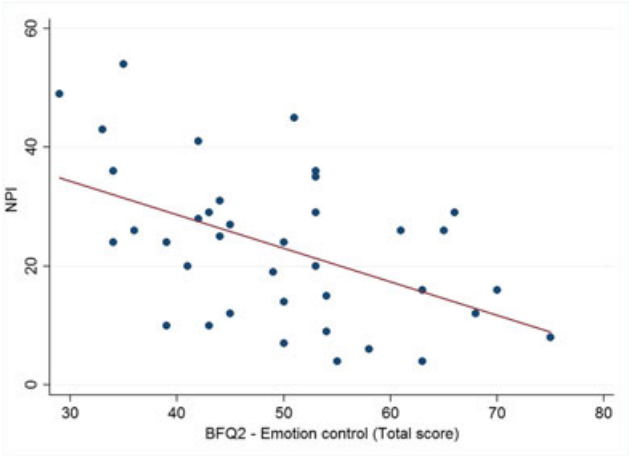

Figure 1 Significant correlation between neuropshychiatric disturbances and BFQ 2- emotion control (total score).

(SD 0.34); mean Cumulative illness rating scale comorbidity index 5.1 (SD 2); mean NPI 23.3 (SD 12.7); CBI mean score was 31 (SD 15.4; range 0–62).

The results showed a significant correlation between emotional stability (for both subitems emotional control [$n = 41$; $r = -0.46$, $P = 0.003$] and impulse control [$n = 41$; $r = -0.34$, $P = 0.032$]) and decreased NPI (Fig. 1), as well as a trend correlation between extroversion/energy total score and increased NPI ($n = 41$; $r = 0.29$; $P = 0.074$). The stepwise regression analysis confirmed a significant correlation between emotional stability (emotional control subitem) and NPI ($P < 0.001$), along with a significant trend between energy/extroversion and increased NPI ($P = 0.04$), adjusting for age ($P = 0.017$). Disease duration was not significantly associated with the clinical outcome.

Despite the aforementioned shortcomings, the present study supported the existence of an association between higher emotional stability, as a negative affect over emotional experience, and decreased BPSD.

Among the strengths of the present study, the original use of a clinometric robust and detailed patients' personality traits (BFOQ2) along with an objective behavioral assessment can be reported. Conversely, the cross-sectional study design and the limited sample of patients were the main limitations.

However, in our opinion, further additional studies are requested to test the potential mechanisms underlying this association in order to include personality traits as a risk factor for BPSD in dementia.

Disclosure statement

The authors declare no conflict of interest.

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Reduced brain-derived neurotrophic factor is associated with cognitive dysfunction in patients with chronic heart failure

Dear Editor,

Chronic heart failure (CHF) is a condition in which the heart is unable to deliver sufficient perfusion to whole organs including the brain, and the elderly population is prone to developing CHF. It is widely known that CHF patients have a higher prevalence of cognitive dysfunction (~75%) and all types of dementia.[1] Brain-derived

neurotrophic factor (BDNF) is a molecule found in high concentration in the hippocampus, and is crucial in memory formation, cell proliferation and synaptic plasticity.[2] The blood BDNF level is lower in CHF patients,[2,3] and could be used as a risk marker for both dementia and CHF.[4–6] However, the association between BDNF and cognitive dysfunction in CHF remains to be elucidated.

We have recently carried out the Brain Assessment and Investigation in Heart Failure Trial, in which we were able to show the cognitive impairment in CHF patients.[7] In the present subanalysis study of the Brain Assessment and Investigation in Heart Failure Trial, we thus examined serum BDNF levels in 40 stage C patients (aged 66.8 ± 8.9 years, 32.5% women) with past or current CHF symptoms, and 40 stage B patients (aged 65.0 ± 10.9 years, 22.5% women) as controls with structural heart disease, but no CHF symptoms following the European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA) guidelines.[8] The present study was approved by the ethics committee of the Tohoku University Graduate School of Medicine, and registered in the University Hospital Medical Information Network (UMIN000008584). Patient characteristics including age, sex, education, ischemic origin, risk factors and medications were comparable between the two groups, as previously reported.[7] Serum BDNF levels, as a secondary end-point, were measured using the BDNF Emax ImmunoAssay System kit (Promega Corporation, Madison, WI, USA). Depressive symptoms, general cognitive functions and immediate (IM) and delayed memory (DM) were assessed using the 15-item Geriatric Depression Scale (GDS), Mini-Mental State Examination (MMSE) and the logical memory subtest of the Wechsler Memory Scale-Revised, respectively. All continuous variables were expressed as mean ± standard deviation (stage C *vs* stage B), and were analyzed by Student's *t*-test. All hypothesis testing was two-sided with a significance level of $P < 0.05$.

The serum BDNF level was significantly lower in the stage C group than in the Stage B group (211.6 ± 161.3 *vs* 409.0 ± 390.6 pg/mL, $P = 0.004$). In the stage C group, univariate regression analysis showed that serum BDNF level was significantly associated with GDS, IM and DM scores. In multivariate regression analysis, stepwise variable selection identified IM score as the best subset of the covariates associated with serum BDNF level. The association between serum BDNF level and MMSE score was also significant in the model that included age, sex, and education (all $P < 0.05$; Table 1). In the stage B group, neither univariate nor multivariate regression analysis showed a significant association. We subsequently carried out a subgroup analysis with a median split between stage C patients with serum BDNF level above and those below the median of 181.3 pg/mL. Serum BDNF level and MMSE score were significantly lower in the low-BDNF group than in the high-BDNF group (BDNF 83.9 ± 60.1 *vs* 339.3 ± 124.4 pg/m:, $P < 0.001$; MMSE 28.1 ± 1.4 *vs* 29.1 ± 0.8, $P = 0.007$), but there were no significant differences in GDS, IM or DM score (GDS 4.2 ± 2.4 *vs* 4.7 ± 2.7, $P = 0.581$; IM 15.5 ± 7.1 *vs* 19.4 ± 7.7, $P = 0.108$; DM 13.4 ± 7.2 *vs* 16.4 ± 7.5, $P = 0.202$). These results show that serum BDNF level is significantly associated with cognitive dysfunction in CHF patients.

BDNF plays a crucial role in memory formation through cell proliferation and synaptic plasticity in the hippocampus, which contains a high concentration of BDNF.[2] We have previously shown that there are structural abnormalities of the hippocampus in a rat model of CHF with a reduction in gray matter, neurogenesis and neurite outgrowth, and an increase in the number of astrocytes.[9] Furthermore, we showed that lower cerebral blood flow in the hippocampus is associated with depressive symptoms and cognitive dysfunction in CHF patients.[7] Thus, reduction in BDNF could cause hippocampus abnormalities with resultant psychological disorders in CHF patients. Lower blood BDNF levels are associated with a higher incidence of dementia and poor prognosis of CHF.[4–6] Of note, exercise training increases blood BDNF levels in healthy individuals, and decreases psychological symptoms and occurrence of death or hospitalization in CHF patients.[10,11] In the present study, serum BDNF levels were significantly different between stage B and C patients, although almost all of them had already received appropriate medical therapy. Thus, an additional intervention, such

Table 1 Regression analysis for brain-derived neurotrophic factor level in stage C heart failure patients

	Multivariate analysis #1				Multivariate analysis #2				Estimate	SE	R^2	*P*-value
	Estimate	SE	R^2	*P*-value	Estimate	SE	R^2	*P*-value				
MMSE	45.6	19.4	0.127	0.024					39.9	19.6	0.216	0.049
GDS	4.0	10.3	0.004	0.697								
IM	8.0	3.2	0.141	0.017	8.0	3.2	0.141	0.017				
DM	7.0	3.4	0.101	0.046								

$n = 40$. Stepwise variable selection was used to identify the best subset of covariates associated with brain-derived neurotrophic factor level in multivariate analysis #1. The model with multivariate analysis #2 was adjusted for age, sex and education. DM, delayed memory; GDS, geriatric depression scale; IM, immediate memory; MMSE, Mini-Mental State Examination; SE, standard error.

as exercise training, might be effective for recovering serum BDNF level with resultant improvement of cognitive dysfunction, dementia and long-term prognosis in CHF patients.

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Femoral osteoporosis is more common than lumbar osteoporosis in patients with Werner syndrome

Dear Editor,

Werner syndrome (WS) is a rare autosomal recessive genetic disorder characterized by early onset of the normal aging processes and its associated complications, including osteoporosis. Mutations in the human *WRN* gene, encoding a member of the RecQ family of DNA helicases, result in this disorder.[1] We aimed to elucidate the clinical characteristics of osteoporosis in WS. A total of 10 patients (5 men and 5 women; mean age 50 years, range 40–60 years) were included. A diagnosis of WS was made based on the presence of the cardinal signs and symptoms of the disease, which include progeroid changes in hair, bilateral cataracts, intractable skin ulcers, soft-tissue calcification, bird-like face and abnormal voice, and was subsequently confirmed by genetic testing (Table 1).[2] Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry using the same machine for all the patients, and osteoporosis was diagnosed based on the Japanese diagnostic criteria for primary osteoporosis (BMD ≤70% of young adult mean or *t*-score ≤−2.5 SD).[3] As judged by lumbar ($L_{2–4}$) BMD, only one of 10 patients (case 1) was diagnosed with osteoporosis (Table 1). In contrast, based on the femoral BMD, six of 10 patients (cases 1, 2, 3, 5, 7 and 10) were diagnosed with osteoporosis (Table 1). Examination of thoracolumbar (T_4–L_4) radiographs showed that none of the patients sustained morphological vertebral fracture, any deformity of lumbar spine and calcification of abdominal aorta. Our present observation indicates that