

NEUROPSYCHIATRY AND BEHAVIORAL NEUROLOGY

Preliminary validation of the Stress and Adversity Inventory for Adults (Adult STRAIN) in Dutch and its associations with in-vivo locus coeruleus integrity

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Abstract

Background: The Stress and Adversity Inventory (STRAIN) systematically assesses lifetime stressor exposure, but its validity has yet to be established in The Netherlands. This work aims to validate the Dutch translation of STRAIN and its association with key biological correlates: cortisol measures and the locus coeruleus (LC), a brain-stem nucleus involved in stress responses and accumulating phosphorylated tau early in adulthood.

Methods: Eighty-seven cognitively unimpaired Dutch participants (31-81 years; ~45% female; Table 1) completed stress- and affective-related questionnaires, cognitive testing, salivary and plasma cortisol measurements, and 7T-MRI. The STRAIN was administered after translation into Dutch. LC MRI signal intensity was extracted from an MT-TFL sequence by normalizing LC signal against the pontine tegmentum (reference region) and creating a sample-specific LC template. Pearson correlation models assessed associations between STRAIN summary scores (total stressor count and severity), and stress-related (MIA-Anxiety, PSS, DASS-Stress, NEO PI-R-Neuroticism), affective (DASS-Anxiety-Depression, HDRS), cognitive (WLTDR, LDST, STR3), stress-related biological (salivary-, plasma cortisol), and LC measures (Table 1). HDRS models employed Spearman correlations. Age and sex were included as covariates, additionally including education for cognitive measures. Analyses were *FDR*-corrected and conducted based on complete cases.

Results: Overall, the sample had relatively low lifetime stressor counts ($M = 14.08$; Figure 1A). When assessing concurrent validity, the STRAIN was positively associated with other stress measures ($r = .21,.36$; $p_{FDR} <.05$; Figure 1B,C). Models including cortisol revealed that less stressor exposure and severity were associated with higher cortisol levels ($r = -.22,-.23$; $p_{FDR} <.05$). Affective and cognitive measures were investigated for discriminant validity. STRAIN was not associated with DASS, but was positively associated with HDRS ($r = .17,.28$; $p_{FDR} <.05$). Generally, greater stressor exposure was related to poorer cognitive performance ($r = .13,-.19$; $p_{FDR} <.05$), except

for a positive association between WLTDR and stressor severity ($r = .18; p_{FDR} <.05$). No significant associations were found with LC MRI signal intensity (Figure 1B).

Conclusion: This study demonstrates preliminary good concurrent and discriminative validity for the Dutch STRAIN translation, even among individuals with low-to-moderate self-reported stress levels. We found no direct associations between LC integrity and lifetime stressors. Future research will investigate associations with other STRAIN domains and potential moderating effects of Alzheimer's Disease-related biomarkers on the relationship between cumulative stressor exposure and LC integrity.

Participant characteristics

n	87
Age	59.17 (13.36, 31-81)
Sex, No. (%) = M	47 (54.0)
Years of Education	14.44 (1.96, 10-20)
APOE-ε4 Carrier Status, No. (%) = ε4	32 (37.2)
MMSE Score	29.05 (1.12, 26-30)
STRAIN Stressor Count Score	14.08 (8.20, 5-57)
STRAIN Stressor Severity Score	30.14 (18.88, 5-114)
MIA - Anxiety Score *	30.98 (7.47, 12-44)
PSS Score *	8.89 (4.70, 0-22)
DASS - Stress Score *	5.16 (4.53, 0-18)
DASS - Anxiety Score ^	1.82 (2.11, 0-13)
DASS - Depression Score ^	2.84 (3.69, 0-17)
NEO PI-R - Neuroticism Score *	121.09 (21.88, 68-180)
HDRS Score ^	2.31 (2.62, 0-12)
WLTDR Score #	9.95 (2.51, 2-15)
LDST Score #	17.95 (3.17, 11-24)
STR3 Score (Reaction time) #	92.72 (22.49, 59.47-167.64)
Salivary Cortisol \$	6.04 (3.76, 1.67-25.91)
Plasma Cortisol \$	0.31 (0.10, 0.08-0.78)
LC MRI signal intensity (a.u.)	0.15 (0.06, 0.08-0.44)

Table 1. Data is presented as numbers and (percentages) or means and (standard deviations, range). Previously validated stress-related questionnaires are indicated in blue*, affective questionnaires in orange^, cognitive measures in yellow#, and stress-related biological measures in green\$. Missing data for APOE-ε4 Carrier Status (n = 1), NEO PI-R - Neuroticism (n = 2), Salivary Cortisol (n = 2), Plasma Cortisol (n = 7), LC MRI signal intensity (n = 7). Abbreviations: M, male; No, number; MMSE, Mini-Mental State Examination; STRAIN, Stress and Adversity Inventory for Adults; MIA, Metamemory in Adulthood; PSS, Perceived Stress Scale; DASS, Depression, Anxiety and Stress Scale; NEO PI-R, Revised NEO Personality Inventory; HDRS, Hamilton Depression Rating Scale; WLTDR, Word Learning Task Delayed Recall; LDST, Letter Digit Substitution Test; STR3, Stroop Color Word Task; LC, locus coeruleus, a.u., arbitrary unit.

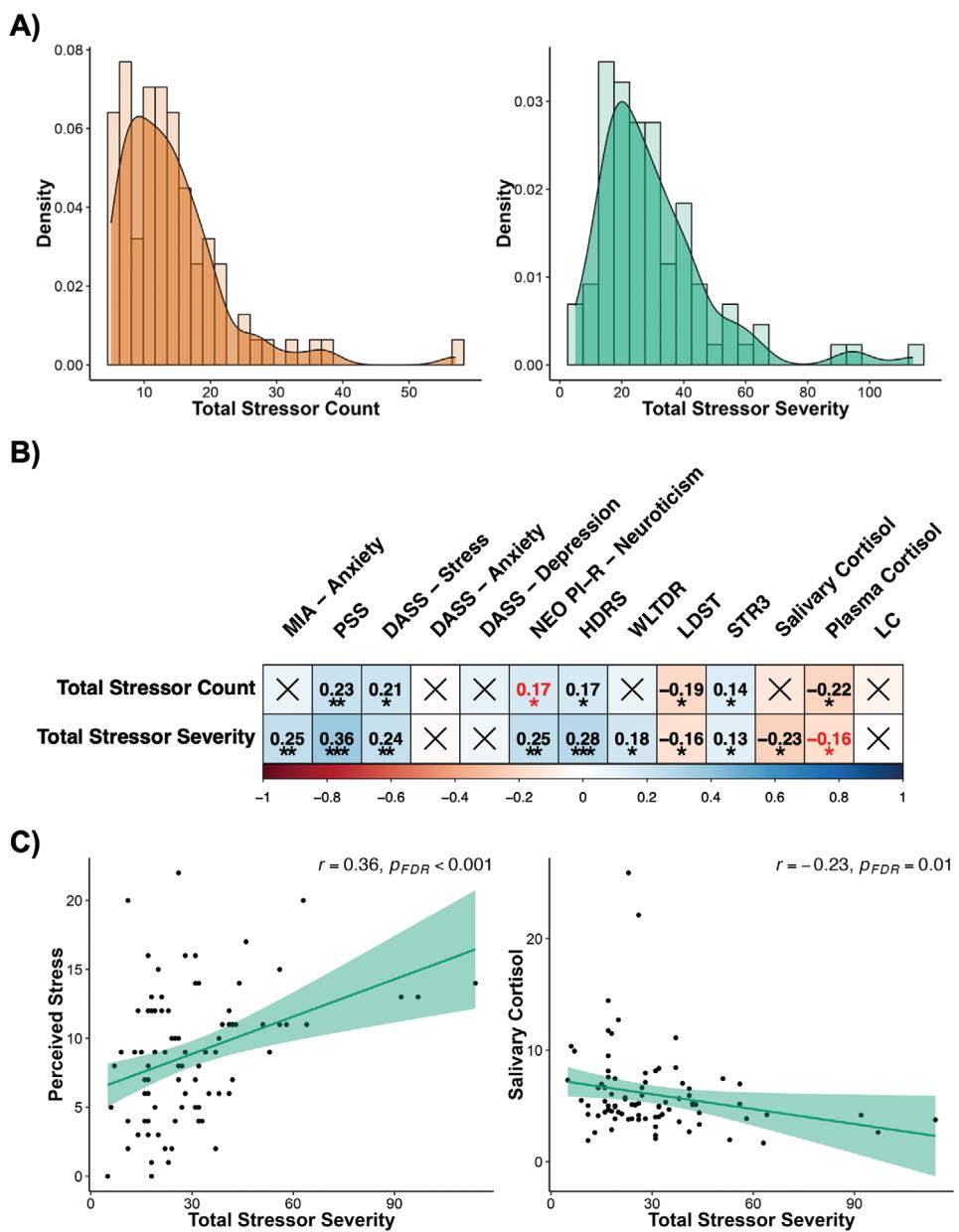


Figure 1. Distributions of the STRAIN summary scores and their associations with various other stress-related, affective, cognitive, and LC measures. A) Density plots of the two principal STRAIN summary scores: Total Stressor Count (left) and Total Stressor Severity (right). **B)** Correlogram depicting partial correlation coefficients and corresponding strength, direction, and significance level of associations between Total Stressor Count and Total Stressor Severity with other stress-related, affective, cognitive, stress-related biological, and LC MRI signal intensity measures. Note that the STR3 cognitive measure is expressed in reaction time. All analyses are corrected for age and sex, and models including cognitive measures are additionally corrected for education. *P*-values in black represent *FDR*-adjusted *p*-values, while *p*-values in red represent unadjusted *p*-values and models that did not survive multiple comparisons correction. * *p*<0.05, ** *p*<0.01, *** *p*<0.001. **C)** Visualization of the positive association between Total Stressor Severity and Perceived Stress Scale (left; *n* = 87; *r* = 0.36; *p*_{*FDR*} < .001), as well as the negative association between Total Stressor Severity and Salivary Cortisol (right; *n* = 85; *r* = -0.23; *p*_{*FDR*} = .010). Abbreviations: MIA, Metamemory in Adulthood; PSS, Perceived Stress Scale; DASS, Depression, Anxiety and Stress Scale; NEO PI-R, Revised NEO Personality Inventory; HDRS, Hamilton Depression Rating Scale; WLTDR, Word Learning Task Delayed Recall; LDST, Letter Digit Substitution Test; STR3, Stroop Color Word Task; LC, locus coeruleus.