

Clinical and biochemical characteristics differentiating chronic fatigue syndrome from major depression and healthy control populations: relation to dysfunction and RNase L pathway.

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Patterns of immune dysfunction have emerged in CFS that include an immune activation state (evidenced by increased activated T lymphocytes and circulating cytokines) and poor cellular function (low natural killer (NK) cell cytotoxicity and impaired T lymphocyte response to mitogens). Therefore, the aim of the current study was to examine the relationship between clinical and functional characteristics, immune abnormalities and status of the RNase L pathway in CFS compared with healthy control and depression control populations.

All study participants were assessed with respect to their general health, functional status, blood count and chemistry, biochemical and immune parameters.

The CFS group (CDC criteria '88 and '94, Karnofsky Performance score <60, n=66) demonstrated clinical, functional and biochemical abnormalities distinct from the healthy (n=62) and depression (n=51) control groups. The CFS group showed marked functional impairment compared with both control groups ($p < .001$) as measured by the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) ($p < .001$). The CFS group also showed decreased cognitive performance on a computerized test battery compared to healthy ($p < .001$) and depression controls ($p < .009$) and significantly higher 37/80 kDa RNase L ratio ($p < .001$) compared with both control groups. The odds ratios of a 37/80 kDa RNase L ratio >2 compared with the CFS patients were 3.9 for the healthy controls ($p < .05$) and 65.8 for the depression controls ($p < .001$). The CFS group demonstrated low NK cell cytotoxicity compared to healthy controls ($p = .045$).

The correlation between abnormalities in the RNase L pathway and impaired NK cell function ($r = .21$, $p < .006$) suggests that both may be part of the same underlying disease mechanism, at least in this homogeneous population of very disabled CFS patients. Healthy contact-control subjects who had exposure to CFS patients showed a number of characteristics similar to the CFS patients, including an increased mean 37/80 kDa RNase L ratio ($p < .04$) and prevalence of the 37/80 kDa RNase L ratio >2 ($p < .03$). In these contact-control subjects, the 37/80 kDa RNase L ratio was correlated with the interferon- α levels ($r = .58$, $p < .02$), suggestive of activation of the interferon pathway.

The results of the present study support the cytokine/immune activation model in this well-characterized CFS patient group.