Additional file 1

Sympathetic nervous system and chronic fatigue syndrome

In literature on chronic fatigue syndrome (CFS), there seems to be no consensus on whether this disorder is characterized by hyperfunction [121], normalcy [122] or hypofunction [123] of the sympathetic nervous system (SNS), although it is generally accepted that CFS patients tend to have some kind of dysfunction of the autonomic nervous system [124,125]. This dysautonomia may present as a combination of abnormally high and low test values obtained from various assays of the SNS and parasympathetic nervous system functions [125,126]. It is known that increased activity of the SNS typically results in vasoconstriction in most tissues (except for brain parenchyma [127] and skeletal muscle), elevated blood pressure, increased heart rate, and an elevated plasma level of norepinephrine (one of the major sympathetic neurotransmitters) [128-130]. Reduced activity of the SNS will usually have the opposite effects [131]. Below is a brief overview of literature on the status of these physiological variables in CFS:

a) Estimates of baseline vascular tone in CFS patients, as measured by total peripheral resistance (mean arterial pressure divided by cardiac output), suggest that there may be a trend toward greater peripheral vasoconstriction associated with CFS [132-134]. On the other hand, the change of peripheral vascular resistance in CFS patients in response to a head up tilt challenge appears to be within the normal range [135].

b) Although many studies report that CFS is often associated with a decrease in blood pressure during either an orthostatic or tilt challenge [124,126,136-139] there are reports of increased blood pressure in CFS patients under somewhat different experimental conditions of head up tilt [133,140]. Baseline blood pressure in CFS patients is within the

normal range according to some studies [139,140] and may be elevated according to others [132].

c) Many studies report development of tachycardia in a significant percentage of CFS patients during an orthostatic or tilt challenge [126,137,139,141]. Baseline heart rate in CFS is within the normal range according to some studies [139,140] and elevated according to others [132,135,142].

d) The baseline level of norepinephrine in plasma appears to be normal [122,143,144], although some studies show elevated levels of norepinephrine in CFS patients [145]. Some studies report exaggerated responses of plasma norepinephrine to standing for 10 minutes [137]. On the other hand, the response of plasma norepinephrine to exercise appears to be within the normal range in CFS [122].

The average age and gender differences among the reports cited above make it rather difficult to compare them directly. Nevertheless, this brief and superficial overview suggests that studies of plasma norepinephrine, heart rate, and peripheral resistance point to either normal or excessive activity of the SNS in CFS patients. On the other hand, data from studies on blood pressure can be interpreted as hyperfunction, normalcy or hypofunction of the SNS in patients with CFS. At present, it is not clear if the SNS disturbances are a causative factor of CFS or a consequence of abnormally low physical activity or some other pathology [124,132,142,146]. Further research would be needed to identify a cause of the observed dysautonomia in CFS.

As mentioned in the text, exposure to cold is known to activate the SNS [130,147] and, depending on experimental conditions, this may result in different cardiovascular responses [148]. Cardiovascular effects of 20°C showers, which are proposed in this paper, have never

been studied (at least cannot be found in PubMed). Somewhat paradoxically, head-out immersion of humans in cold water at 20°C *lowers* both blood pressure and heart rate [148] despite significant peripheral vasoconstriction and a more than 4-fold increase in plasma norepinephrine [149]. Since immersion in thermoneutral water (32-34°C) has an almost identical inhibitory effect on blood pressure and heart rate [148] (while it does not increase peripheral vasoconstriction and plasma norepinephrine [150]), it is possible that the cardiovascular response to 20°C water immersion is due to immersion in water rather than exposure to cold. Therefore, cold showers at 20°C may not have a detectable effect on blood pressure and heart rate. Alternatively, a 20°C cold shower may cause an increase in blood pressure and a decrease in heart rate as observed in experiments with exposure to cold air [151]. It should be noted that immersion in colder water (at 14°C) increases both heart rate and blood pressure [130,148]. Systemic exposure to cold (different methods) has not been reported to cause a detectable change in the plasma level of epinephrine [130,152,153]. Finally, repeated exposure to cold does not appear change the baseline level of norepinephrine in healthy test subjects [130].

In conclusion, it is not clear if physiological stimuli that activate the SNS (such as exposure to cold) will have a net beneficial or a net adverse effect on patients with CFS. As mentioned in argument #6, graded exercise appears to benefit CFS patients [154,155] despite transient activation of the SNS during exercise [156]. Therefore, daily brief exposure to cold may or may not aggravate the autonomic nervous system abnormalities that are often observed in CFS patients.

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