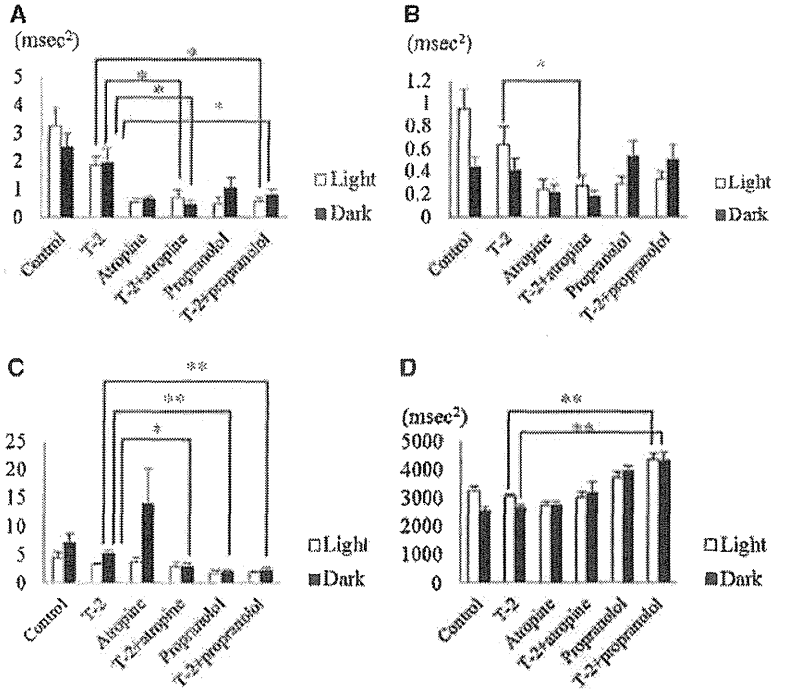

Figure 8. Changes in the value of power spectrum of heart rate variability in response to 0.5 mg/kg T-2 toxin with blockades. (A) low-frequency (LF) power; (B) high-frequency (HF) power; (C) LF/HF ratio; (D) total power. Asterisks: significant difference ($*p < 0.05$, $**p < 0.01$) from the T-2 toxin (0.5 mg/kg) group. Data are based on mean values obtained for each 2 or 3 days and expressed as means ± SEM.

immediately after T-2 toxin administration. Instead, they predominantly appeared after 8 h, and the arrhythmias lasted for the three days of observation after the T-2 toxin administration. This finding indicates that T-2 toxin administration takes time to produce an arrhythmogenic condition in the rat's heart and that the cardiac influence lasted for at least three days. Similarly, in our previous study, DON, which is one of mycotoxins in the trichothecene group, also induced arrhythmia that was exhibited mostly at 10–20 h after toxin administration (Ngampongsa et al. 2011). Although it is feasible to consider that direct toxic effects (Bunner and Morris 1988) on myocytes were associated with the occurrence of arrhythmia, most of the second-degree AV blocks and sinus bradycardia in the present study seemed to be induced or augmented by the vagal activity since such a conduction disturbance was largely diminished by the atropine treatment.

If T-2 toxin induced hypotension for a few days following administration of T-2 toxin, it should provoke a reflex inhibition of the vagal activity and augmentation of the sympathetic nerve activity. From the results of an acute experiment in the dog, the reduction in arterial blood pressure and increase in heart rate were suggested to be mediated by the sympathetic nervous system (Bubien and Woods 1987). In the present study, it was assumed that the tonus of the parasympathetic nervous activity was enhanced intermittently to regulate heart rate and systemic blood pressure by means of antagonistic neural mechanisms during basically high tension of the sympathetic nervous activity for a longer period after the administration of T-2 toxin. Such events of parasympathetic activation might cause a momentary decrease in firing rate at the sinoatrial node and also produce second-degree AV blocks, which lead to a slowing of atrioventricular conduction.

The causal relationship between arrhythmias and the decrease in LF, HF and total powers observed at 0.5 mg/kg of T-2 toxin in the present study was unclear. Although the arrhythmias such as sinus bradycardia and atrioventricular blocks are considered to be associated with momentary alteration of balance between the sympathetic and parasympathetic nervous activities, such nervous activities may be not necessarily reflected the HRV analysis.

A significant increase in occurrence of ventricular extrasystoles was identified with the combination of 0.5 mg/kg-T-2 toxin and atropine. The increase in heart rate results in an elevation in workload of the heart and might produce cardiac conditions tending to cause ventricular extrasystoles. It is known that tachycardia produces an accumulation of superoxide anion released from the mitochondrial electron transport chain in myocytes (Han et al. 2001). In addition, T-2 toxin itself has been clarified to be a substance producing oxidative stress in tissues involving the brain (Chaudhari et al. 2009; Chaudhary and Rao 2010; Doi and Uetsuka 2011). Although the detailed mechanism of ventricular extrasystoles observed in the present study was not elucidated, the oxidative stress, to some extent, may be attributed to this arrhythmia, as it has been reported that the number of cases of ventricular extrasystole in cases

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of myocardial reperfusion was significantly decreased by treatment with superoxide dismutase (Kónya et al. 1992).

In conclusion, the results of the present study demonstrated and confirmed that T-2 toxin has a property of potent cardiac toxicity, the appearance of which was largely influenced by the autonomic nervous activity, lasting for at least three days in conscious rats with a concentration of 0.1 mg/kg or more administered subcutaneously.

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Declaration of interest

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