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Commentary

Cardiorespiratory arrest in a healthy volunteer after a single oral dose of 80 mg of the beta-blocker propranolol

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The oral administration of a single low-to-moderate dose of propranolol (30–80 mg) in young healthy volunteers is widely used to probe the brain's (nor)adrenergic system (for example as published in NLM: Oei, Tollenaar, Elzinga, & Spinhoven, 2010; Tollenaar, Elzinga, Spinhoven, & Everaerd, 2009; Van Stegeren et al., 2007). Propranolol, a beta-adrenergic antagonist, is an effective tool for investigating the role of the beta-adrenergic system in psychological processes of interest. It is typically used in a placebo-controlled design to parcel out the contribution of the beta-adrenergic system. The common side effects of propranolol, a drop in pulse rate and blood pressure, are well known and typically well endured. However, it is less known that in rare cases the oral administration of a single dose of propranolol may induce cardiorespiratory arrest in healthy young volunteers.

We describe a case of a young healthy volunteer without any known pre-existing medical condition, who participated in a challenge study and suffered a non-fatal cardiac arrest after oral administration of a single dose of 80 mg propranolol. We used a double-blind pseudo-randomized placebo-controlled crossover design of two consecutive days to investigate the effect of modulation of the beta-adrenergic system on different components of the EEG pattern. The protocol was approved by the Medical Ethical Committee of the Leiden University Medical Center and subjects gave written informed consent. A blood pressure in rest below 100/60 mmHg or a pulse rate of less than 60 beats per minute (BPM) were exclusion criteria for the study. The study was performed in the Department of Psychology of Leiden University. Based on prior extensive experience with this paradigm (Oei et al., 2010; Tollenaar et al., 2009; Van Stegeren et al., 2007) and advice from internists, only a physician on call with knowledge of the protocol was deemed necessary.

The healthy volunteer was an eighteen-year-old male student, who was the last of the 20 subjects scheduled to participate in our experiment. He had no past or current history of cardiac, pulmonary or other physical diseases. There had been no prior exposure to a beta-blocker. The family history mentioned the death of a grandfather at the age of 45, possibly due to a cardiac arrest. The other grandfather had cardiac valve surgery at older age. The volunteer was an active sportsman. He was member of a rowing competition team and trained four times a week and he also played football. He was a non-smoker and used no drugs. He used 2 units of alcohol per day. Routine physical examination showed no neurological, cardiac or pulmonary abnormalities. The subject had a blood pressure of 120/65 mmHg with a regular pulse rate of 60 BPM while sitting, and a tension of 120/70 mmHg with a pulse rate of 65 BPM while standing.

The volunteer arrived in the morning of the first test day. Blood pressure at baseline was 140/69 mmHg, with a pulse rate of 63 BPM. The volunteer received an oral dose of 80 mg propranolol (blinding was broken on his test day). Thirty minutes after baseline the blood pressure was 141/64 mmHg, with a pulse rate of 49 BPM. The volunteer felt as usual and was e-mailing. Subsequently, he was accompanied to and placed in the EEG set-up. The volunteer complained of being hungry and hot, and then collapsed. He stopped breathing and there were convulsions. The researchers immediately called an ambulance as well as the physician on call. Meanwhile the volunteer had already regained consciousness and had a blood pressure of 110/65 with a pulse rate of 50 BPM. After arrival of the emergency personnel and the physician, ECG monitoring was started and atropine administered intravenously. However, the volunteer collapsed again and stopped breathing, and there was a short asystolic period, ended by a precordial thump. He almost immediately regained consciousness again. After intravenous administration of more atropine and physiological salt the bradycardia disappeared and the blood pressure rose. The volunteer was transferred to the cardiology department for further observation and evaluation. Both echography and 24-h ECG revealed no abnormalities. The cardiologist's conclusion was cardiorespiratory arrest due to propranolol. The following day the volunteer was discharged in good condition, without the need for any further follow-up.

There are many reports in the literature on cardiorespiratory arrest after oral administration of propranolol in cardiopulmonary compromised patients or in the case of an overdose. We could, however, not identify any recent reports of cardiorespiratory arrest in healthy young volunteers after oral administration of a single dose of propranolol. Our case report indicates that besides careful screening of healthy subjects in experiments involving the oral administration of a single dose of propranolol, it is also necessary to have trained staff and equipment for resuscitation available at the test site.

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