Whole Body Vibration and Spatial Learning: c-Fos and ChAT as Neuronal Correlates of Cognitive Improvements

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It has been well established that physical activity (exercise) by way of running wheel or treadmill activity improves motor and cognitive performance in (sedentary) mice [1,2,3]. This type of exercise, however, cannot be performed well by aging mice or mice with motor deficiencies. Notably the amount of voluntary exercise of old mice in running wheels decreases largely (up to 90% as compared to young mice). Here, we aimed to find an alternative type of exercise and examined whether whole body vibration (WBV) as a form of passive exercise can improve motor and cognitive performance. WBV stimulates the entire body, including brain, via controlled vibrations as used in human power plates. A scale model was build for mice, by which different frequencies and g-forces could be applied to mice [4]. The mice were placed in a cage which was directly connected to the vibrating platform of the vibrator located in the middle of the cage. Mice received WBV for 5 weeks, 10 minutes per day, week days only. Pseudo-WBV was performed by placing the mice in the cage in the absence of the actual vibrations. WBV continued during the days of testing, but was always performed after the behavioral testing was done at the end of the day in order to prevent acute effects of WBV on behavior. No signs of distress or anxiety were observed during the 10 minutes of WBV treatment. In NMRI mice, three frequencies (20, 30 and 45 Hz) and two g-forces (0,2 and 1,9 g) were compared for the capacity to improve motor performance, using rotarod, hanging wire and balance beam as tests. Best motor performance was found at 30 Hz and 1,9g [4]. Thereafter, these settings were used as standard, and the balance beam test the standard test for motor performance. Next, C57BL6 or CD1 mice (3 or 24 months of age) received these mild vibrations. WBV improved sensory-motor abilities as measured in the balance beam test, irrespective of age and strain. Learning and reversal learning in a Y maze was used as a spatial learning task. Results in C57Bl6 mice showed a significant improvement in Y-maze learning (rate of acquisition), but no improvement in Y-maze reversal learning [3]. A direct comparison of WBV, running wheel and treadmill activity revealed that the cognitive improvement in the Y maze by WBV, although somewhat less, was of a similar degree as induced by the active forms of exercise. WBV in CD1 mice failed to show significant improvement in the Y maze, in contrast to the improvement of motor performance. The improvements in motor performance due to WBV developed at a slower in old than young subjects. To examine the neurophysiological brain changes induced by WBV treatment, c-Fos and ChAT immunoreactivity was measured in experimentally naïve young C57Bl6 or CD1 mice after 1, 3, and 5 weeks of WBV, and one day after 5 weeks of WBV. Pseudo-WBV treatment served as control. The results showed that hippocampal c-Fos expression gradually and strongly increased in C57Bl6 mice after 1, 3 or 5 weeks, but only marginally in CD1 mice. c-Fos expression was back to baseline values one day after the last WBV session. The pattern of c-Fos expression in the brain, with areas reacting in varying degree from highly activated to no change, suggests that sensory stimulation via the whiskers is a primary pathway by which WBV stimulates the brain [5]. Strong increases in c-Fos staining were observed in hippocampal CA1 and CA3 regions and the prefrontal cortex, among others. In contrast to c-Fos, no significant WBV-induced changes were found for Arc or Egr1/zif268. Immunoreactivity for choline-acetyltransferase (ChAT), the acetylcholine synthesizing enzyme, was measured in the nucleus basalis, medial septum, hippocampus, neocortex and amygdala (C57Bl6 mice only). No WBV-induced changes were found in the nucleus basalis, whereas significant increases were found in the medial septum. The WBV-induced increase in the medial septum was lost one day after the last WBV session, but remained present in hippocampus, neocortex and amygdale. The ChAT data suggests increased cholinergic responsiveness due to WBV, like described for physical exercise [6]. Significant changes in the hippocampal ChAT staining, probably contributing to cognitive improvements, developed slightly slower than the improvements in motor performance. This suggests that WBV is slightly more effective in improving sensory-motor abilities than spatial learning abilities. Taken together, these findings indicate that WBV as a form

of passive exercise is suitable for improving cognitive performance in young and old subjects. It also suggests that c-Fos and ChAT are WBV-specific neuronal correlates serving a 'priming' of the septohippocampal circuit for improved acquisition of spatial learning. A next step.we made was to study the effect of WBV on cognitive performance in humans. Recent studies at our University within a consortium of Life Sciences, Movement Sciences and Neuropsychology revealed that WBV significantly improves cognitive performance (Stroop test). Taken together, our data clearly shows the potential of WBV as an intervention to improve motor and cognitive performance in subjects not able (or willing) to perform active forms of exercise. This is of particular interest to aging human subjects in need of an alternative, non-aerobic type of exercise.

References

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