

Music During Awake Brain Tumor Resection: A Case Series

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To the Editor:

Awake brain tumor resection is an essential method for treating patients with tumors adjacent to eloquent brain regions, especially those important for language function. Intraoperative cortical and subcortical brain mapping, as well as comprehensive language and neuropsychological assessments, allow and optimize the extent of tumor resection while minimizing the risk of permanent neurological deficits.^{1,2} Patients undergoing awake brain tumor resection often experience anxiety, which can increase sympathetic nervous activity and affect anesthetic efficacy, wound healing, and the recovery process.^{3–5} Thus, reducing stress during surgery is critical to improving patient outcomes. Music therapy is a nonpharmacological intervention that has shown promise in reducing stress in a variety of medical settings.^{6,7} This prompted us to investigate whether exposure to patient-preferred music could be beneficial in reducing stress in awake patients undergoing tumor resection.

To investigate the potential benefits of intraoperative music as a stress-reduction strategy, a prospective case series was conducted in 10 patients undergoing awake resection of glioma at the Department of Neurosurgery, University Hospital Mannheim. Ethical approval was

obtained on March 12, 2019, from the Medical Ethics Committee II, Faculty of Medicine Mannheim, University of Heidelberg, Germany, 2019-638N. Written informed consent was obtained from all participants. Patient demographics and characteristics are provided in Supplemental Digital Content 1 (<http://links.lww.com/JNA/A861>). For awake brain tumor resections, our institutional asleep–awake–asleep anesthesia protocol is illustrated in the combined schematic and workflow (Supplemental Digital Content 2, <http://links.lww.com/JNA/A862>).

To enhance patient comfort and minimize anxiety-related effects, we designed a setup tailored to awake surgery, which isolates patients from operating room noise while allowing them to listen to self-selected music (music selection by the patient, Supplemental Digital Content 3, <http://links.lww.com/JNA/A863>) with intermittent interruptions for speech assessment. In addition, we provide exclusive communication channels between the speech therapist and primary neurosurgeon using a digital communication system with microphones for both the speech therapist and the patient, adjustable noise-canceling headphones, and a sound system with a mixing console. Synchronized iPads were used to support speech testing, one placed in the patient's field of view and the other used by the speech therapist to present speech assessment slides (Figure: Setup, equipment, and workflow for music-induced physiological monitoring, Supplemental Digital Content 2, <http://links.lww.com/JNA/A862>).

This prospective case series aimed to compare stress levels during episodes with music intervention to those without music intervention. To enable intraindividual comparisons, a 5-minute baseline period without music was recorded after dural opening and initial speech testing, but before cortical or subcortical mapping and tumor resection, and before the start of music exposure. This was followed by a 5-minute music exposure period. This design allowed for the examination of cardiac autonomic regulation in both conditions, providing insight into the potential benefits of music during awake brain tumor resections.

Objective stress levels were measured using oscillatory heart rate variability (HRV) derived from heart rate measurements, a reliable indicator of autonomic nervous system function^{8–10} (Fig. 1; Supplemental Digital Content 4, <http://links.lww.com/JNA/A864>; HRV measurements; Supplemental Digital Content 5, <http://links.lww.com/JNA/A865>; NN intervals during awake tumor resection with music

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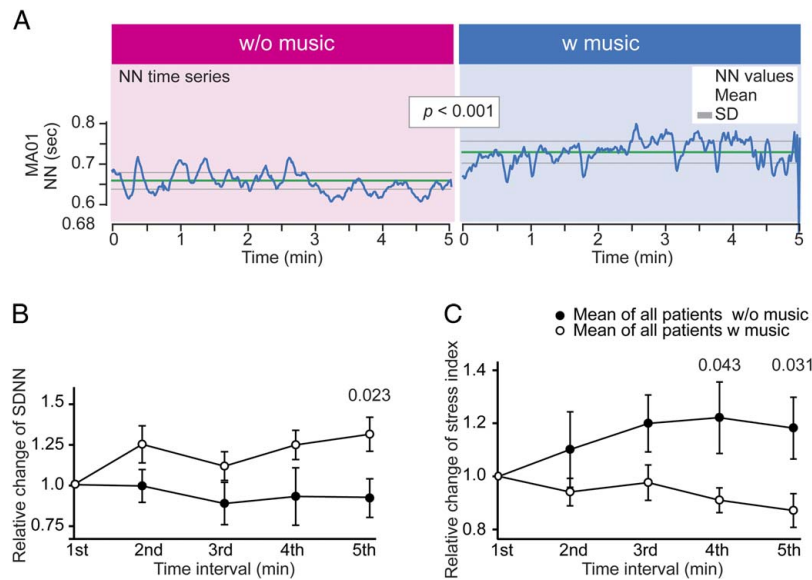


FIGURE 1. Music exposure during awake brain tumor resection is associated with reduced physiological stress. A, Representative NN interval trace (blue line) for patient MA01 during 2 consecutive 5-minute periods without (red background) and with (blue background) music exposure. Green line: mean NN interval; grey band: SD. Statistical comparison performed using Student *t* test. B and C, Mean relative changes in SDNN (B) and Kubios Stress Index (C) across five 1-minute intervals. Solid dots: without music; outlined dots: with music. Error bars: SEM. Statistical comparison performed using Student *t* test. SDNN indicates SD of normal-to-normal; NN, normal-to-normal.

exposure; Supplemental Digital Content 6, <http://links.lww.com/JNA/A866>: Intraoperative heart rate and NN intervals). Under conditions of mental equilibrium and reduced anxiety, HRV maintains a continuous oscillation, reflecting a balanced sympathovagal state. A decrease in HRV indicates an imbalance in the patient’s autonomic nervous system. HRV data were collected using a 3-lead electrocardiogram (ECG) and analyzed using Kubios HRV software (v3.3.1). To identify and eliminate potential artifacts, a threshold-based beat correction was set to 0.3, resulting in artifact-free normal-to-normal (NN) interval data.¹¹

In addition to NN interval data, key HRV indices were used to quantify autonomic responses. These indices included SD of NN intervals (SDNN; Fig. 1B) and the Kubios stress index (Fig. 1C), which allows evaluation of both parasympathetic and sympathetic activity in response to the music intervention^{9,12} (Supplemental Digital Content 4, <http://links.lww.com/JNA/A864>: HRV measurements).

As there is high between-subject variability of HRV measures, we normalized the trajectory values to the HRV measure recorded during the first 1-minute interval, with and without music exposure, respectively.

SigmaPlot (Systat Software Inc. 14.0) was used for statistical analysis. The Brown-Forsythe test was used to test for equal variance of continuous variables. Group comparisons were performed using Student *t* test and Mann-Whitney *U* test. A threshold of *P* < 0.05 was considered significant.

All patients verbally reported that the inclusion of music had a calming effect on their emotional state during surgery when asked, although no formal patient-reported outcome measure or questionnaire was used.

Consistent with these subjective reports, listening to music resulted in a significant decrease in heart rate, and consequently a significant increase in NN interval, in 8 out of 10 patients (Fig. 1A, Supplemental Digital Content 5: NN intervals during awake brain tumor resection with music exposure).

The pooled comparative analysis of heart rate showed a significant decrease when comparing the awake phase without music accompaniment (93 ± 18 bpm) to the following 5-minute time interval with music exposure (85 ± 13 bpm; *P* < 0.001); consequently, the of NN intervals showed a significant increase of 54.3 ms during the music intervention (*P* < 0.001; Supplemental Digital Content 6). In grouped analysis, we observed significant changes in different HRV stress measures, indicating an overall reduction in sympathetic activity, specifically in SDNN and the Kubios stress index over time (Fig. 1B, C). These changes in HRV suggest that music exposure during awake brain tumor resection may have contributed to a more relaxed autonomic state in patients.

This preliminary case series has several limitations. The small sample size and lack of a comparison group limit the generalizability of the findings. In addition, changes in heart rate and HRV during surgery may be influenced by multiple factors, including surgical stage, anesthetic administration, and patient-specific variables such as beta-blocker use. Moreover, we did not collect patient-reported outcomes to more accurately characterize patient experience during these procedures.

Future studies should employ a larger, randomized controlled design incorporating both physiological stress

markers and validated patient-reported outcomes. A brief version of the State-Trait Anxiety Inventory,¹³ may be particularly suitable for intraoperative use. Additional physiological measures for consideration include EEG,¹⁴ salivary alpha-amylase,¹⁵ electrodermal activity and skin conductance,¹⁶ as well as peripheral indicators such as breathing rate, skin temperature, muscle activity, and pupil diameter.

This prospective case series provides preliminary evidence that music may reduce stress during awake brain tumor resection. If substantiated in larger studies, the integration of patient-preferred music could enhance patient-centered care as a simple, cost-effective intervention.

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