



## Letter to the Editors

**Where words fail, music speaks: Isolated memory processes in a musical patient with schizophrenia**

Dear Editor,

Processing rule-governed knowledge recruits the procedural memory system rooted in frontal/basal-ganglia circuits, whereas processing memorized idiosyncratic knowledge depends on temporal lobe regions involved in declarative memory (Ullman, 2001). These or related systems likely underlie rule- and memory-based processes in both language and music (Langheim et al., 2002; Patel, 2003; Miranda and Ullman, 2007). Miranda and Ullman (2007) found that “out-of-key” notes – constituting violations of musical tonality rules in familiar and unfamiliar melodies – elicited similar neural responses to grammar rule violations in language, whereas unexpected “in-key” notes in familiar melodies elicited a pattern of brain activity associated with lexical–semantic processing. Tasks requiring detection of violations can reveal whether putative deficits in patients are associated with processing rule-based (procedural) or memorized (declarative) knowledge.

We explored these distinct music memory processes in a 31-year-old individual with noteworthy musical aptitude against a backdrop of widespread cognitive impairment and psychotic symptoms (auditory and visual hallucinations, thought broadcasting, and paranoia) due to schizophrenia. The patient was treated with aripiprazole, clozapine, lithium, and sertraline. Extensive neuropsychological testing – as part of the “CBDB/NIH Sibling Study” – revealed performance under the 30th percentile in most domains, including intelligence, graphomotor speed, episodic verbal memory, long-term lexical and semantic retrieval, and working memory. Despite these deficits, the patient played guitar and sang dozens of popular tunes without apparent difficulty.

To characterize the specific nature of the patient's spared musical ability, we tested responses to musical violations (task adapted from Miranda, 2007). Sixty melodies (5–18 s in length) were presented: thirty well-known and thirty novel tunes, matched for musical complexity. Half of the melodies contained a note violation (out-of-key or in-key) that lasted 600 ms. Out-of-key violations in both well-known and novel melodies were inconsistent with musical tonality rules. In-key violations in well-known melodies followed rhythmic and tonal rules but violated the familiar

(memorized) version of the melody. The patient listened to each melody and either pressed a button marked “bad” as soon as a violation was detected, or waited until the end of the tune and pressed a button marked “good.” After each tune, the patient indicated orally whether or not it was familiar. Only well-known melodies rated by the patient as familiar, and novel melodies rated as unfamiliar, were analyzed.

The patient's performance was compared to previously collected data from 29 healthy volunteers: 16 “musicians” (as defined by training and/or performance experience) and 13 “non-musicians” (Miranda, 2007). Musicians were significantly more accurate than non-musicians at detecting each violation type ( $p < .05$ ). Given the patient's musical aptitude, we predicted proficient identification of out-of-key note violations requiring processing of rule-governed information. In contrast, the patient's poor verbal and semantic retrieval led us to predict impaired identification of in-key but “incorrect” notes in familiar tunes, which relies upon intact representations of memorized melodies using declarative memory.

The patient recognized fewer well-known melodies (63%) than non-musicians (73%,  $SD = 15%$ ) and musicians (84%,  $SD = 9%$ ), but correctly judged novel melodies as “unfamiliar” (93%) at a similar rate to control groups (non-musicians: 88%,  $SD = 8%$ ; musicians: 88%,  $SD = 8%$ ). The patient was highly accurate at identifying out-of-key violations in both familiar and unfamiliar melodies, similar to musicians. However, the patient was notably poorer than both control groups in detecting in-key violations in familiar melodies (see Fig. 1).

The patient's recognition of fewer tunes and difficulty identifying in-key violations in familiar melodies suggests impaired memorization or processing of idiosyncratic knowledge, consistent with a declarative memory deficit. The patient's spared detection of out-of-key violations suggests preserved processing of rule-governed information, at least in the domain of music. During musical performances (e.g., playing guitar and singing), the patient may have relied on musical rules to overcome memory impairments, given that production of music (e.g., learning sequences of motor movements to play the guitar) is believed to depend at least in part on procedural memory (Pascual-Leone, 2001). It is possible that repeated practicing of songs and their lyrics allowed the patient's guitar playing and singing to become proceduralized, and thus more efficiently recalled.

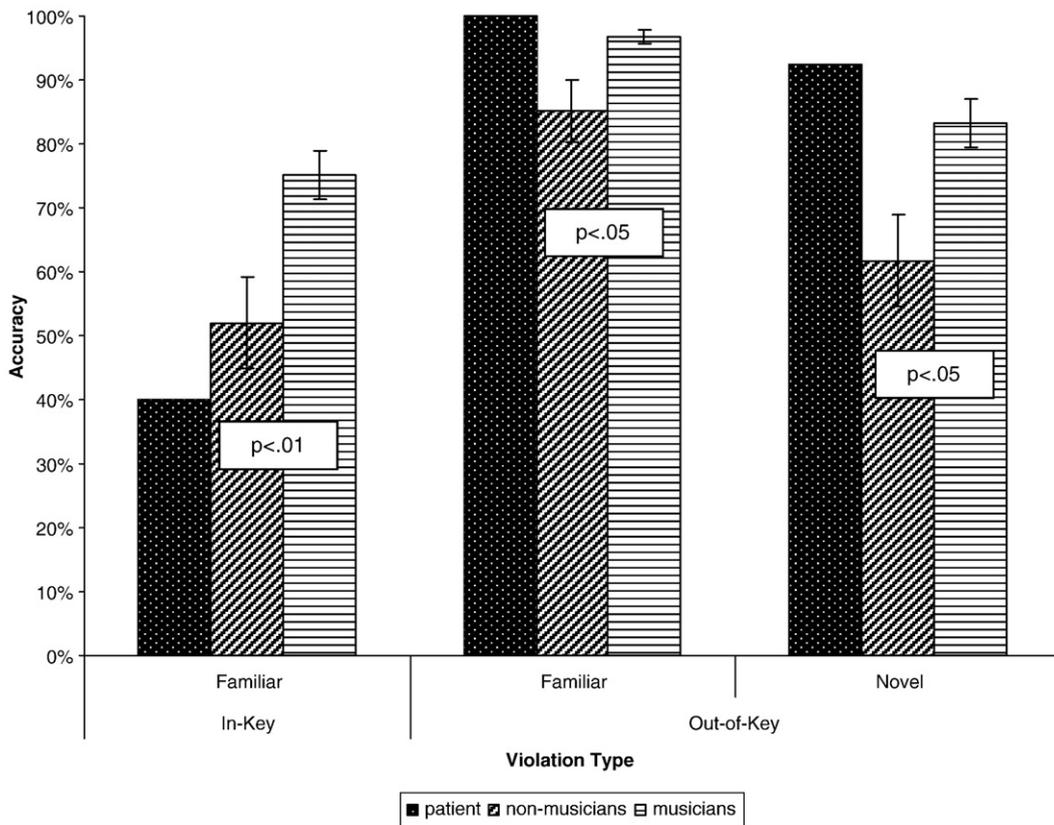


Fig. 1. Accuracy of melody familiarity ratings in the patient, non-musicians and musicians.<sup>1</sup>

The patient's data within the musical domain parallels findings in verbal and nonverbal domains, with impaired declarative memory but preserved implicit memory in schizophrenia (Goldberg et al., 1990; Weickert et al., 2002). However, the nature and specificity of this preservation remains controversial (Siebert et al., 2008).

To our knowledge, this case study is the first to investigate aspects of both rule-based (procedural) and memorized (declarative) processing of music in schizophrenia. The preservation of the former but not the latter may have implications not only for elucidating the cognitive processes underlying schizophrenia, but also for treatment. For example, music therapy has been shown to improve mental state, negative symptoms and social functioning in patients with schizophrenia (Gold et al., 2005). The findings of our study warrant further exploration of the processing of rule- vs. memory-based aspects of music and other domains in schizophrenia.

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#### References

- Gold, C., Heldal, T., Dahle, T., Wigram, T., 2005. Music therapy for schizophrenia or schizophrenia-like illnesses. The Cochrane Database of Systematic Reviews (2).
- Goldberg, T.E., Saint-Cyr, J.A., Weinberger, D.R., 1990. Assessment of procedural learning and problem solving in schizophrenic patients by Tower of Hanoi type tasks. *J. Neuropsychiatry Clin. Neurosci.* 2, 165–173.
- Langheim, F.J., Callicott, J.H., Mattay, V.S., Duyn, J.H., Weinberger, D.R., 2002. Cortical systems associated with covert music rehearsal. *Neuroimage* 16, 901–918.
- Miranda, R. (2007). Double dissociation between rules and memory in the neurocognition of music. Ph.D. dissertation, Georgetown University Medical Center, United States – District of Columbia. Retrieved July 17, 2008, from Dissertations & Theses @ Georgetown University – WRLC database. (Publication No. AAT 3283076).
- Miranda, R.A., Ullman, M.T., 2007. Double dissociation between rules and memory in music: an event-related potential study. *Neuroimage* 38 (2), 331–345.
- Pascual-Leone, A., 2001. The brain that plays music and is changed by it. *Ann. N.Y. Acad. Sci.* 930, 315–329.
- Patel, A.D., 2003. Language, music, syntax and the brain. *Nat. Neurosci.* 6 (7), 674–681.
- Siebert, R.J., Weatherall, M., Bell, E.M., 2008. Is implicit sequence learning impaired in schizophrenia? A meta-analysis. *Brain Cogn.* 67 (3), 351–359.
- Ullman, M.T., 2001. A neurocognitive perspective on language: the declarative/procedural model. *Nat. Rev., Neurosci.* 2, 717–726.
- Weickert, T.W., Terrazas, A., Bigelow, L.B., Malley, J.D., Hyde, T., Egan, M.F., Weinberger, D.R., Goldberg, T.E., 2002. Habit and skill learning in schizophrenia: evidence of normal striatal processing with abnormal cortical input. *Learn Mem.* 9, 430–442.

<sup>1</sup> *p* values were calculated using *t*-tests for significance (*df* = 27) between non-musicians and musician control groups for each violation type. Error bars show standard error.

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