Aus der Klinik für Neurologie
der Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

Untersuchungen zum musikalischen Gedächtnis bei einem professionellen Cellisten mit amnestischen Syndrom

zur Erlangung des akademischen Grades
Doctor medicinae (Dr. med.)

vorgelegt der Medizinischen Fakultät
Charité – Universitätsmedizin Berlin

von
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Datum der Promotion: 30.05.2015

2. Abstrakt in Deutsch:

Ein amnestischer professioneller Cellist mit intaktem Musikgedächtnis

Lernen und Gedächtnis von Musik beruht auf einer Vielzahl von perzeptuellen, motorischen, affektiven und mnestisch-autobiographischen Prozessen. Patientenstudien und bildgebende Studien weisen darauf hin, dass dem musikalischen Gedächtnis möglicherweise eigene neuronale Substrate zu Grunde liegen könnten. Aktuell wird kontrovers diskutiert, inwieweit Musikgedächtnis unabhängig von anderen Gedächtnisprozessen organisiert ist. Wir untersuchten das musikalische Gedächtnis eines professionellen 68-Jahre alten Cellisten („Patient PM“), der aufgrund einer Herpes-Enzephalitis ein schweres amnestisches Syndrom entwickelt hatte. In wiederholten bildgebenden Untersuchungen des Gehirns waren ausgedehnte Gewebsnekrosen des Temporallappens bilateral unter Einschluss des Hippokampus nachgewiesen worden. Diese Konstellation bot die einzigartige Gelegenheit, das musikalische Gedächtnis eines Patienten zu untersuchen, der ein genau definiertes prämorbides musikalisches Wissen hatte.

In einer ausführlichen Batterie mit etablierten neuropsychologischen Tests untersuchten wir zunächst verbale und visuelle Gedächtnisinhalte sowie Arbeitsgedächtnis. Hier zeigte PM schwerste Defizite für semantische und episodische Gedächtnisinhalte in allen getesteten Bereichen. Anschließend testeten wir PM’s musikalische Fähigkeiten mit einer etablierten Testbatterie (Montreal Battery of Evalution of Amusia; MBEA). Hier zeigte sich, dass nicht nur die perzeptuellen musikalischen Leistungen intakt waren, sondern auch das Gedächtnis für einfache musikalische Inhalte. Wir entwickelten daraufhin drei Tests, die den Beginn der Gedächtnisstörungen unseres Patienten berücksichtigten und die sowohl das retrograde als auch das anterograde Musikgedächtnis untersuchten. Die Kontrollgruppe bestand aus aktiven Amateurmusikern und professionellen Musikern der Berliner Philharmoniker. In allen Aufgaben wurden kurze Ausschnitte klassischer Instrumentalstücke paarweise präsentiert. In Aufgabe 1 wurden Stücke, die vor 2005 - und somit vor Beginn der Amnesie des Patienten - komponiert worden waren gemeinsam mit nach 2005 komponierten Stücken präsentiert. Die Musikstücke

waren hinsichtlich Charakter, Stimmung und Instrumentierung gematcht. Die Probanden wurden instruiert, das bekanntere Stück zu benennen. In Aufgabe 2 wurden zwei Musikstücke aus der gleichen Musikepoche präsentiert (komponiert vor 2005), jeweils ein bekanntes und ein unbekanntes Werk. In der dritten Aufgabe wurde das anterograde Musikgedächtnis untersucht. Hierzu mussten die Probanden unbekannte, noch nicht gehörte Stücke von kurz zuvor gehörten Stücken unterscheiden. Erstaunlicherweise zeigte PM im Vergleich zur Kontrollgruppe in allen drei Aufgaben eine intakte Musikgedächtnisleistung. In weiteren Kontrollexperimenten, die das Erinnern nonverbaler Stimuli (Gesichter, Objekte) erforderten, zeigte PM hingegen ein ausgeprägtes Gedächtnisdefizit.

Zusammenfassend zeigen diese Untersuchungen, dass Lernen und Gedächtnis musikalischer Informationen tatsächlich von neuronalen Netzwerken abhängen, die sich zumindest partiell von den Netzwerken für andere episodische und semantische Gedächtnisinhalte unterscheiden. Läsionsanalysen von PM und Ergebnisse früherer Studien deuten hierbei auf den rechten Gyrus temporalis superior als ein mögliches zentrales Substrat für musikalisches Gedächtnis.

3. Abstrakt in Englisch:

Preservation of musical memory in an amnesic professional cellist

Learning and memory of music involves a multitude of perceptual, motor, affective, and autobiographical memory processes. Patient and imaging studies suggest, that musical memory may involve distinct neural substrates. However, the degree of independence from other memory domains is controversial. We have investigated a 68-year-old professional cellist, patient PM, who developed severe amnesia following encephalitis. Repeated imaging studies demonstrated extensive bilateral lesions of the temporal lobes, including the hippocampal formation. This constellation provided a unique opportunity to study musical memory in a patient with a precisely defined premorbid musical knowledge.

With an extensive battery of established neuropsychological tests, we examined verbal and visual memory as well as working memory. Here, PM demonstrated severe deficits of semantic and episodic memory in every tested domain. Subsequently, we tested PM's musical abilities with an established test battery (Montreal Battery of Evaluation of Amusia; MBEA). Not only perceptual musical abilities were unaffected, but also PMs memory for simple musical material. Hereupon we developed three tests that took the onset of his encephalitis into account and which were designed to examine his retrograde and his anterograde musical memory. The control group consisted of active amateur musicians and professional musicians of the Berlin Philharmonic Orchestra. In each task, short excerpts of classical instrumental music were presented pairwise. In a first task, musical excerpts composed before 2005, i.e. before the onset of PM's amnesia, were presented pairwise with excerpts composed after 2005. Excerpts were matched with respect to character, mood and instrumentation. Subjects were instructed to name the more famous composition. In a second task, we presented two musical excerpts composed in the same musical era (all composed before 2005), a well-known and an unknown excerpt. In a third task, we tested anterograde musical memory. Subjects were requested to differentiate between excerpts of completely unknown musical compositions, and excerpts of unknown compositions they had just previously listened to for the first time. Surprisingly, PM showed normal performance in each of the three tasks. In control experiments, that required the ability to memorize nonverbal stimuli, PM demonstrated a severe memory deficit.

In summary, these findings suggest that learning and long-term retention of musical information depends on brain networks, that are at least partially distinct from networks involved in other types of episodic and semantic memory. Lesion analyses of PM and results of previous studies point to the right superior temporal gyrus as a possible substrate for musical memory.

4.1 Eidesstattliche Versicherung

„Ich, Nazli Esfahani-Bayerl, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema “ Untersuchungen zum musikalischen Gedächtnis bei einem professionellen Cellisten mit amnestischen Syndrom” selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung (siehe „Uniform Requirements for Manuscripts (URM)“ des ICMJE -www.icmje.org) kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) entsprechen den URM (s.o) und werden von mir verantwortet.

Mein Anteil an der ausgewählten Publikation entspricht dem, der in der untenstehenden gemeinsamen Erklärung mit dem Betreuer angegeben ist.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§156,161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

_____ _____

Datum Unterschrift

4.2 Ausführliche Anteilserklärung an der erfolgten Publikation

Publikation:

Carsten Finke*, Nazli E. Esfahani* and Christoph J. Ploner, Preservation of musical memory in an amnesic professional cellist, Current Biology 2012

Die Arbeit beinhaltete drei selbstentwickelte Tests für musikalisches Gedächtnis. Das musikalische Stimulusmaterial bestand aus mehr als 300 Auszügen von komponierter Instrumentalmusik, die bezüglich verschiedener musikalischer Parameter gematcht wurden. Es wurden darüber hinaus selbst entwickelte Tests für visuelles Stimulusmaterial angewandt.

Es wurden für den Patienten PM ein alters-gematchtes Vergleichskollektiv mit professionellen Musikern der Berliner Philharmoniker und ein weiteres Vergleichskollektiv mit altersentsprechenden Laienmusikern zusammengestellt.

Ich habe das musikalische Material für die Testungen zusammengesucht, Auszüge aus den Stücken geschnitten, sämtliche verwandte Stimuli programmiert und die Stimuli schließlich in Form einer Testbatterie zusammengestellt. Anschließend wurden sämtliche Stimuli und der grundsätzliche Versuchsablauf an einem gesundem Kollektiv von mir erprobt und dann von mir an PM und den an beiden oben genannten Vergleichskollektiven getestet. Weiterhin habe ich das Material für die visuellen Gedächtnis-Tests zusammengesucht und zu einer Testbatterie zusammengestellt um diese ebenfalls an PM und beiden Vergleichskollektiven zu testen.

Darüberhinaus habe ich an sämtlichen Probanden eine Batterie mit etablierten neuropsychologischen Tests und eine Batterie zur Testung elementarer musikalischer Teilleistungen angewandt. Nach Erhebung wurden sämtliche Daten von mir unter Anleitung statistisch analysiert.

Die Projektidee entstand im Rahmen von Vorarbeiten der Arbeitsgruppe Brain & Behavior zu Gedächtnisdefiziten bei Läsionen des Temporallappens, an denen ich ebenfalls beteiligt war und in dessen Kontext wir auf den Patienten PM aufmerksam wurden. Von der ersten Idee bis zum endgültigen Vorliegen der Daten dauerte das Projekt zwei Jahre. In diesem Zeitraum habe ich mich dem Projekt während eines

Freisemesters vollzeitig sowie während drei weiteren Semestern mit erheblichem Zeitaufwand studienbegleitend gewidmet.

Mein Promotionsprojekt wurde beim Jahrestreffen der Society for Neuroscience in Washington 2011 in einer Pressekonferenz der Society vorgestellt und hat ein nachhaltiges Echo in der internationalen Presse und dem Internationalen Rundfunk gefunden. Die Publikation wurde zum Paper des Jahres 2012 des CSB (Centrum für Schlaganfallforschung) der Neurologie der Charité gewählt.

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Unterschrift, Datum und Stempel des betreuender Hochschullehrer

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Datum/Unterschrift der Doktorandin

5. Auszug aus der Journal Summary List

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				Total Cites	Impact Factor	5-Year Impact Factor	Immediacy Index	Articles	Cited Half-life	*Eigenfactor*® Score	*Article Influence*® Score
☑	1	CELL	0092-8674	178762	31.957	34.366	6.499	415	8.5	0.58533	19.272
☑	2	ANNU REV BIOCHEM	0066-4154	19420	27.681	31.964	4.312	32	>10.0	0.05109	17.412
☑	3	NAT MED	1078-8956	57350	24.302	27.139	5.763	186	7.8	0.16402	12.390
☑	4	MOL CELL	1097-2765	47818	15.280	14.902	2.818	296	6.2	0.22828	8.708
☑	5	MOL PSYCHIATR	1359-4184	12686	14.897	13.985	3.879	116	5.3	0.04215	5.060
☑	6	GENOME RES	1088-9051	28856	14.397	14.104	3.416	238	5.7	0.13170	7.473
☑	7	ACTA CRYSTALLOGR D	0907-4449	12453	14.103	7.540	0.604	182	6.6	0.04782	3.751
☑	8	TRENDS BIOCHEM SCI	0968-0004	15642	13.076	12.005	2.406	64	9.5	0.03850	5.770
☑	9	NAT CHEM BIOL	1552-4450	10819	12.948	15.600	3.715	130	3.8	0.06736	7.304
☑	10	PLOS BIOL	1545-7885	22908	12.690	13.447	2.151	152	5.2	0.13390	7.451
☑	11	NAT STRUCT MOL BIOL	1545-9993	24299	11.902	12.307	2.576	184	6.2	0.12272	7.588
☑	12	MOL SYST BIOL	1744-	6335	11.340	12.392	1.877	57	3.8	0.04313	5.979

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☑	13	MOL ASPECTS MED	0098-2997	3016	10.375	10.821	1.462	39	5.4	0.00842	3.325
☑	14	MOL BIOL EVOL	0737-4038	32168	10.353	11.221	1.561	294	6.3	0.09519	4.046
☑	15	PROG LIPID RES	0163-7827	3893	10.250	10.690	1.583	24	8.0	0.00817	3.626
☑	16	NAT PROD REP	0265-0568	6609	10.178	10.072	2.385	65	5.9	0.01745	3.132
☑	17	EMBO J	0261-4189	75950	9.822	9.602	2.553	333	>10.0	0.16016	5.172
☑	18	TRENDS MOL MED	1471-4914	5945	9.571	10.142	1.487	76	5.4	0.02163	3.834
☑	**19**	**CURR BIOL**	**0960-9822**	**43191**	**9.494**	**10.445**	**2.307**	**371**	**6.8**	**0.16637**	**5.551**
☑	20	CURR OPIN CHEM BIOL	1367-5931	8869	9.471	9.256	0.987	76	6.1	0.02624	3.238

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				Total Cites	Impact Factor	5-Year Impact Factor	Immediacy Index	Articles	Cited Half-life	*Eigenfactor*® Score	*Article Influence*® Score
☑	21	TRENDS MOL MED	1471-4914	5945	9.571	10.142	1.487	76	5.4	0.02163	3.834
☑	22	CURR BIOL	0960-9822	43191	9.494	10.445	2.307	371	6.8	0.16637	5.551
☑	23	PLANT CELL	1040-4651	39067	9.251	10.125	1.526	325	8.0	0.08843	3.795
☑	24	CYTOKINE GROWTH F R	1359-6101	4587	8.831	7.919	0.588	34	7.2	0.01086	2.801
☑	25	CURR OPIN STRUC BIOL	0959-440X	10116	8.738	9.020	1.452	93	7.2	0.03683	4.584
☑	26	CELL DEATH DIFFER	1350-9047	14551	8.371	8.395	2.279	190	5.5	0.04934	3.105
☑	27	STEM CELLS	1066-5099	18253	7.701	8.368	1.297	269	5.0	0.06738	2.734
☑	28	SCI SIGNAL	1937-9145	5168	7.648	7.603	1.478	182	2.8	0.04051	3.624
☑	29	CURR OPIN GENET DEV	0959-437X	8178	7.470	8.209	1.538	80	6.8	0.03333	4.377
☑	30	ONCOGENE	0950-9232	60526	7.357	7.180	2.218	458	7.7	0.14406	2.759

☑	31	J MOL CELL BIOL	1674-2788	651	7.308	8.271	1.757	37	2.0	0.00342	2.799
☑	32	EMBO REP	1469-221X	10574	7.189	7.396	1.687	99	6.1	0.04598	3.877
☑	33	ONCOTARGET	1949-2553	1450	6.636	6.636	1.316	114	1.8	0.00645	1.894
☑	34	SEMIN CELL DEV BIOL	1084-9521	5613	6.202	6.510	1.034	116	4.6	0.02624	2.862
☑	35	CELL DEATH DIS	2041-4889	1481	6.044	6.044	0.565	191	2.0	0.00643	1.629
☑	36	STRUCTURE	0969-2126	12441	5.994	6.081	1.466	191	7.6	0.04443	3.253
☑	37	AGEING RES REV	1568-1637	1965	5.953	6.549	1.439	41	4.0	0.00623	1.938
☑	38	J CELL SCI	0021-9533	40261	5.877	6.375	1.032	535	8.0	0.10608	2.883
☑	39	PIGM CELL MELANOMA R	1755-1471	3385	5.839	5.434	1.397	68	6.2	0.00995	1.992
☑	40	AGING CELL	1474-9718	4134	5.705	6.415	1.485	130	4.5	0.01748	2.333

Preservation of musical memory in an amnesic professional cellist

Carsten Finke*, Nazli E. Esfahani*, and Christoph J. Ploner

Learning and memory of music involves a multitude of perceptual, motor, affective, and autobiographical memory processes [1]. Patient and imaging studies suggest that musical memory may involve distinct neural substrates [2,3]. However, the degree of independence of such a system from other memory domains is controversial [4]. We have investigated a 68-year-old professional cellist, patient PM, who developed severe amnesia following encephalitis. This case provided a unique opportunity to study musical memory in a patient with a precisely defined premorbid musical knowledge and well-demarcated focal lesions of the brain. Despite severe memory impairments, he performed like healthy musicians in various tests of recognition memory for music. These findings suggest that learning and retention of musical information depends on brain networks distinct from those involved in other types of episodic and semantic memory.

Throughout his career, PM had performed in major German orchestras and had gained a wide repertoire that ranges from early to contemporary music. In 2005, PM was affected by herpes encephalitis, causing lesions of the right medial temporal lobe, large portions of the left temporal lobe and parts of left frontal and insular cortex (see Figure S1 and Table S1 in the Supplemental Information available on-line with this issue). PM was left with a severe and persistent ante- and retrograde amnesia. Neuropsychological testing revealed an exceedingly poor performance in most subtests of the Wechsler Memory Scale, with relative sparing of short-term memory tasks (Table S2). Moreover, in a systematic interview, PM showed profound deficits in semantic and episodic memory. For example, he could not remember the name of any German river or chancellor. He was neither able to report biographical details from childhood, youth or adulthood, nor other personal or professional events. PM had no memory of relatives and friends, except for his brother and his full-time caregiver. He was unable to recall or recognize lyrics of well-known folk and childrens songs. PM could not recall any famous cellist and remembered the name of only one composer (Beethoven). However, PM was still able to sight-read and to play the cello.

To test PM's musical abilities in more detail, we employed an established battery of tests for evaluation of amusia (Table S3). PM performed normally in all subtests assessing music perception. Surprisingly, he also showed normal performance in a subsequent incidental memory test for single-phrase melodies presented in the battery. To systematically investigate whether musical memory was truly intact in PM, we devised three tasks that took

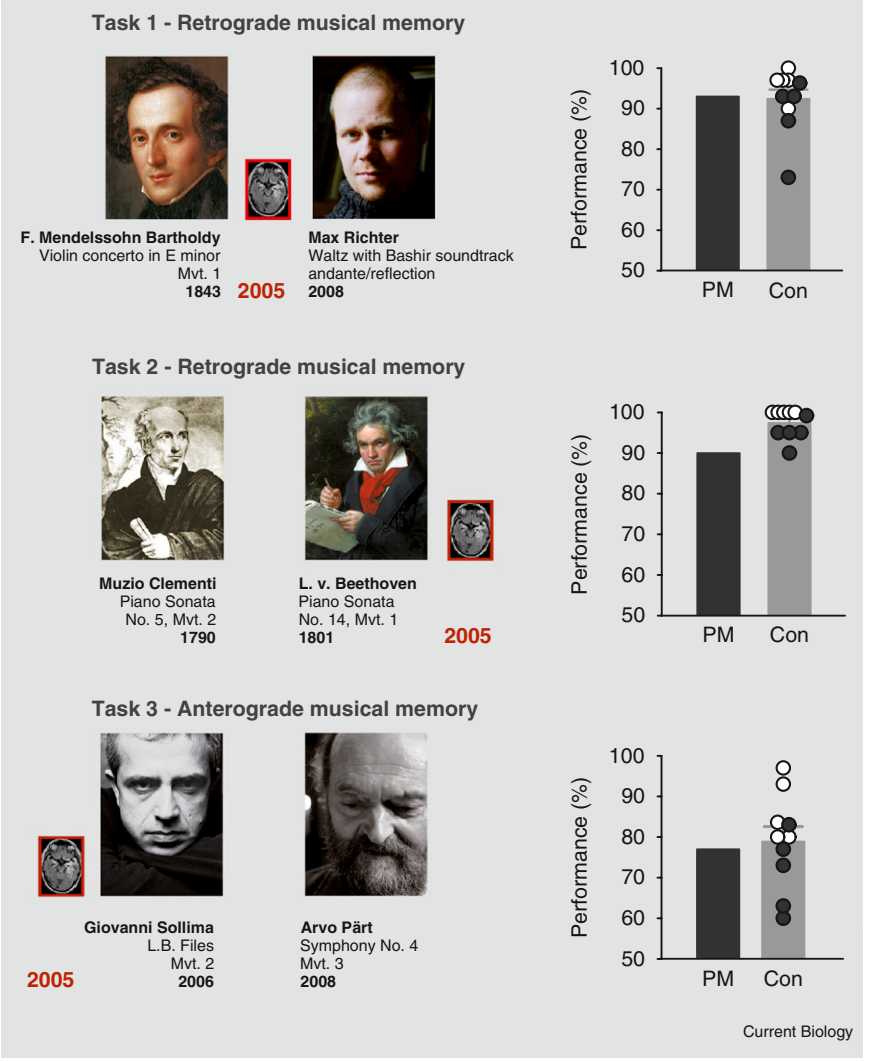

Figure 1. Schematics of the three musical memory tasks and corresponding performance of PM and control subjects.
Subjects listened to matched pairs of instrumental classical music and had to decide which excerpt sounded more familiar. Pieces were closely matched for musical character and instrumental line-up. White dots, Berlin Philharmonic string players; grey dots, active amateur musicians; error bars indicate s.e.m. Top row: retrograde musical memory. Subjects were presented classical music composed before 2005 (before the onset of PM's amnesia) paired with classical music composed after 2005 (after the onset of PM's amnesia). Middle row: retrograde musical memory. Subjects were presented famous and non-famous classical music composed before 2005 and in the same musical period. Bottom row: anterograde musical memory. First, subjects were asked to evaluate the emotional character of musical excerpts composed after 2005. In an incidental memory task 90 minutes later, subjects had to discriminate the previously rated excerpts from matched new excerpts.

the onset of his amnesia into account (Figure 1). Five age-matched string-players from the Berlin Philharmonic Orchestra and five age-matched active amateur musicians served as controls. First, we presented excerpts of well-known instrumental music composed before 2005 — so before the onset of PM's amnesia — paired with excerpts of instrumental music composed after 2005. These foils were matched with respect to musical character and instrumental line-up. PM discriminated targets from foils at the same level as the control group (93% *versus* 92 ± 2.5% (mean ± s.e.m.), $p = 0.94$).

To rule out that recognition of these excerpts was mediated by subtle differences in compositional style rather than by musical memory, we devised a second task, in which well-known instrumental classical pieces were matched to unfamiliar instrumental pieces of the same musical period (i.e. targets and foils composed before 2005). Although PM's continuous involvement with music had ceased since his encephalitis, he still discriminated famous from non-famous pieces at a level similar to controls (90% *versus* 97 ± 1.1%, $p = 0.07$). In a third task, we assessed PM's ability to learn new complex musical material. In an incidental memory task, where all targets and foils were composed after 2005, subjects were asked to discriminate instrumental pieces from closely matched pieces they had heard 90 minutes before. Again, PM performed at the same level as controls (77% *versus* 79 ± 3.7%, $p = 0.88$).

PM's performance in these musical memory tests was at the same level as a control group composed of amateur and professional musicians (see Supplemental Information for subgroup comparisons). To investigate whether his intact performance was part of a preserved supra-modal semantic memory for non-verbal material or modality-specific, PM was tested in anterograde recognition memory tasks for faces and objects. In both tasks, PM performed significantly worse than controls (faces, 55% *versus* 91 ± 1.9%, $p < 0.001$; objects, 50% *versus* 99 ± 1.2%, $p < 0.0001$). Further analysis confirmed a significant dissociation between musical and non-musical memory domains (music *versus* faces, $p = 0.0005$; music *versus* objects, $p = 0.00004$).

In patient PM, learning and memory of complex musical information constitute an island of intact cognition within a severe amnesic syndrome. Representation of PM's exceptional premorbid musical knowledge and the ability to acquire new musical information survived damage to brain regions implicated in other types of memory surprisingly well. Both the degree of the dissociation between musical and non-musical memory domains and the preservation of explicit musical memory set PM apart from previous studies in amnesic patients with less focal disorders that mostly reported selective preservation of implicit musical memory [4]. Functional imaging studies support the hypothesis that semantic memory of music recruits a distinct and extensive bilateral network in temporal neocortex and prefrontal cortex [2], regions that were partly spared in PM. However, whether this system can be functionally separated from other semantic memory networks is controversial [5]. In particular, investigations of musical memory in patients with Alzheimer's disease (AD) and other dementias have yielded conflicting results. While some studies in AD patients showed that recognition of excerpts of familiar music and recognition of recently learned melodies was impaired together with other semantic and episodic memory domains [4], relative preservation of musical knowledge has been reported in other patients with AD and semantic dementia [6]. Extending these observations, the findings in PM show with particular clarity that the representation of music in the human brain is distinct and largely independent from other explicit memory modalities.

A reverse behavioral pattern to PM has been observed in non-musician patients with bilateral damage to the auditory association cortex [3]. Direct electrical stimulation of this region predominately in the right hemisphere has been shown to elicit musical hallucinations that relate to a subjects' previous musical experience, even after removal of the ipsilateral hippocampus [7]. Comparison of PM's lesion with these data and recent imaging studies [8] suggests that rostral temporal lobe structures in the right hemisphere, rather than the medial temporal lobe, mediate musical memory.

Although it is possible that lifelong musical training has contributed to the preservation of PM's musical memory, the functional and structural dissociation reported here has theoretical and pratical implications. It may be speculated that the particular relevance of music for the development of language and its important social functions may have driven the formation of a dedicated musical memory system in the human brain [9]. Preservation of musical knowledge and learning abilities may not only enhance quality of life in patients with otherwise compromised memory functions, but may also help to meet non-musical everyday challenges [10].

Supplemental Information

Supplemental Information includes one Figure, three Tables and Supplemental Experimental Procedures and can be found with this article online at doi: 10.1016/j.cub.2012.05.041.

Acknowledgements

We thank Ute A. Kopp for neuropsychological assessment of PM. Supported by the Deutsche Forschungsgemeinschaft (DFG PI 248/4-1).

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Supplemental information:

Preservation of musical memory in an amnesic professional cellist

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Supplemental Results

Figure S1. MRIs (01/2005 and 06/2005) and CT scan (07/2010) of PM. Note the bilateral lesion to the medial temporal lobes with additional involvement of left orbitofrontal cortex and large portions of the left temporal lobe (including the rostral superior, middle, and inferior temporal gyri, the temporal pole, and the insula). Images are shown in radiological convention (L, left; R, right).

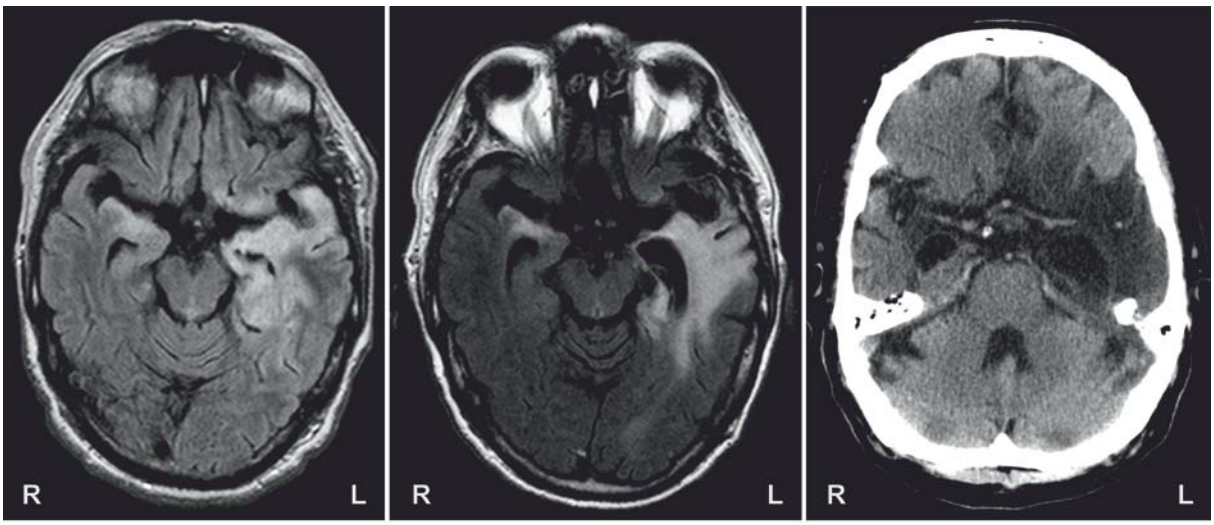

Table S1. Cerebral lesions of patient PM ("-" indicates intact, "+" indicates lesion)

	right	left
medial temporal lobe		
hippocampus		
rostral	+	+
caudal	-	+
entorhinal cortex	+	+
perirhinal cortex	-	+
parahippocampal cortex	-	+
transverse gyrus of Heschl	-	-
rostral	-	(+)
caudal	-	-
superior temporal gyrus		
rostral	-	+
caudal	-	-
middle temporal gyrus		
rostral	-	+
caudal	-	-
inferior temporal gyrus		
rostral	-	+
caudal	-	-
temporal pole	-	+
insula	-	+
inferior frontal gyrus, opercular part	-	+

Table S2. Neuropsychological assessment of PM's memory.

Wechsler Memory Scale-Revised (WMS-R, German Version [S1])

	Score	**Max. Score**	**Index Score** (mean 100, s.d. 10)
General Memory	42	193	< 50 (> 5 s.d. below control mean)
Visual Memory	34	69	75 (2.5 s.d. below control mean)
Verbal Memory	8	124	< 50 (> 5 s.d. below control mean)
Delayed Memory	0	119	< 50 (> 5 s.d. below control mean)

Short-term/working memory

	Score	**Max. Score**	**Percentile rank**
Digit span forward	6	12	28
Digit span backward	6	12	53
Block span forward	7	14	28
Block span backward	6	12	27

Table S3. Performance of PM in the Montreal Battery of Evaluation of Amusia (MBEA, [S2]). The MBEA is a well-established battery that was developed to comprehensively assess musical skills of individuals with cognitive dysfunction. The MBEA includes five tests that assess music perception (melodic variations: contour, interval, scale; temporal variations: rhythm, meter) and a subsequent incidental memory test. All tests use the same pool of 30 novel musical phrases that were composed according to the rules of the Western tonal system.

	Scale	Contour	Interval	Rhythm	Meter	Memory
PM	28	27	22	26	29	24
HC mean ± s.d.*	27 ± 2.3	27 ± 2.2	26 ± 2.4	27 ± 2.1	26 ± 2.9	27 ± 2.3
Cut-off score*	22	22	21	23	20	23

* Data from 160 healthy controls; reproduced from Peretz et al. [S2]

Supplemental Experimental Procedures

Musical Memory Tasks (Task 1 – 3)

Music was played using a Laptop with portable speakers in a quiet room. Volume was adjusted according to the participants' need. Excerpts of musical pieces consisted of the main theme and were ~ 20 s in duration. Targets and foils were played successively with a short pause; all excerpts were only played once. In pairwise presentations, target and foils were presented in a randomized order.

Task 1 (retrograde musical memory)

Thirty excerpts of well-known pieces of instrumental classical music composed before 2005, i.e. before the onset of PM's amnesia, were presented and paired with pieces of instrumental classical music composed after 2005 (Fig. 1). Targets were taken from a web-based list of the 100 most popular pieces of classical music. Foils were carefully matched with respect to musical character (e.g. composition style, mood, tempo) and instrumental line-up independently by two professional musicians. Because PM hardly listened to music after the encephalitis, except for rare occasions when he listened to some of his own recordings, we are confident that he was not familiar with any of the foils before testing. Subjects were asked to indicate the piece that sounded more familiar in a forced-choice task design.

Task 2 (retrograde musical memory)

This task served as control task for task 1. Despite careful matching in task 1, differences in compositional style could have influenced a subjects' decision. We therefore matched 21 well-known pieces of instrumental classical music to 21 unfamiliar pieces of instrumental classical music from the same musical era. Again, targets were taken from a list of the 100 most popular pieces of classical music. Pieces were again matched with respect to musical character and instrumental line-up by two professional musicians. All pieces used in task 2 were composed before 2005.

Task 3 (antegrade musical memory)

Thirty pieces of instrumental classical music composed after 2005 were presented (i.e. music unknown to PM, see above). Subjects first were asked to rate the pieces' emotional character by assigning them to one of the categories joyful, scary, peaceful, threatening and solemn/ceremonial. In an incidental memory task 90 minutes later, these 30 emotionally rated excerpts had to be discriminated from 30 matched new excerpts composed after 2005. Pieces were again matched with respect to musical character and instrumental line-up by two professional musicians.

Task 1 (retrograde musical memory) - List of compositions.

Composer	Work	Year
Satie, E.	Gymnopédie no. 1	1888
Giacchino, M.	Ratatouille soundtrack, main theme	2007
Rossini, G. A.	Il barbiere di Siviglia, overture	1816
Sollima, G.	L.B. Files (mvt 1)	2006
Smetana, B.	My Fatherland, The Moldau (2nd symphonic poem)	1872
Desplat, A.	Chéri soundtrack, The Rose Acacia	2009
Beethoven, L. v.	Piano sonata no. 14, op. 27, no. 2, 'Mondschein' (mvt 1)	1801
Muhly, N.	The Reader soundtrack, Who was She	2008
Monteverdi, C.	L'Orfeo, Toccata	1609
Portman, R.	The Duchess soundtrack, main theme	2008
Bizet, G.	Carmen, Prelude	1875
Rombi, P.	Angel soundtrack, Success	2007
Schubert, F.	Symphony no. 8, 'Unvollendete Symphonie' (mvt 1)	1822
Weihrauch, S.	Elizaveta Bam, scene 8	2007
Williams, J.	Schindler's List soundtrack, main theme	1993
Newman, T.	The good German soundtrack, Unrecht oder Recht	2006
Wagner, R.	Rienzi, overture	1842
Zimmer, H.	Inception soundtrack, Time	2010
Mozart, W. A.	Symphony no. 40 (mvt 1)	1788
Young, C.	Creation soundtrack, To Emma	2009
Mendelssohn Bartholdy, J. L. F.	Violin concerto in E minor, Op. 64 (mvt 1)	1843
Richter, M.	Waltz with Bashir soundtrack, andante/reflection	2008
Händel, G. F.	Feuerwerksmusik, HWV 351, overture	1749
Powell, J.	How to train your dragon soundtrack, See You tomorrow	2010
Prokofiev, S. S.	Romeo & Juliet, Montagues and Capulets, Dance oft the Knights	1935
Newman, T.	The Good German soundtrack, Kraut Brain Trust,	2006
Bach, J. S.	Orchester suite no. 3, BWV 1068, Air	1718
Sollima, G.	L.B. Files (mvt 2)	2006
Schnebel, D.	String quartet, Im Raum (mvt 2)	2006
Vivaldi, A.	Le quattro stagioni, L'Inverno, op. 8	1725
Mussorgski, M. P.	Pictures at an Exhibition, Promenade	1874
Adams, J.	Doctor Atomic Symphony (mvt 3)	2007
Beethoven, L. v.	Bagatelle No. 25, „Für Elise"	1810
Tiersen, G.Y.	Tabarly soundtrack, 8 mm	2008
Strauss, R.	Also sprach Zarathustra, Sonnenaufgang, op. 30	1896
Sylvestri, A,	Night at the museum soundtrack , To Washington	2006
Saint-Saëns, C.	Le carnaval des animaux, aquarium	1886
Reich, S.	Mallet Quartet, (mvt 1)	2009
Rachmaninow, S. W.	Rhapsody on a theme Of Paganini, Op. 43 Var. 18	1934
Desplat, A.	The curious case of Benjamin Button soundtrack, main theme	2009
Desplat, A.	Coco avant Chanel soundtrack, Chez Chanel	2009
Jarre, M.	Doctor Zhivago Soundtrack, Lara's Theme	1965
Dvořák, A.	Cello concert op. 104 (mvt 1)	1896
Glass, P.	Songs and Poems for Solo Cello, Song 3	2006
Beethoven, L. v.	Symphony no. 5, op. 57 (mvt 1)	1808
Dodd, N.	Treasure Island soundtrack, main theme	2006
Barber, S.	Adagio for strings, op. 11	1936
Zimmer, H.	Da Vinci Code soundtrack, Chevalier de Sangreal	2006
Ravel, M.	Boléro	1928
Zimmer, H.	Pirates of the Carrabean, The Brethren Court	2008
Desplat, A.	The Queen soundtrack,Tony and Elizabeth	2006
Strauss, J.	Wiener Blut, Waltz, op. 354	1873
Bell, J., Zimmer, H.	Angels and Demons soundtrack, 503	2010
Mahler, G.	Symphony no. 5, Adagietto (mvt 4)	1904
Lai, F.	Love Story soundtrack, main theme	1970
Eastwood, C.	Changeling soundtrack, end theme	2008
Rimsky-Korsakov, N.	Tale of Tsar Saltan, Flight of the Bumblebee	1900
Gubaidulina, S.	Glorious Percussion (mvt 1)	2008
Steiner M.	Gone with the Wind soundtrack, Tara's theme	1939
Giacchino, M.	Up soundtrack, Carl goes up	2009

Task 2 (retrograde musical memory) - List of compositions.

Composer	Work	Year
Strauss, J.	Wiener Blut, waltz, op. 354	1873
Lumbye, H.C.	Memories from Vienna, waltz	1845
Beethoven, L.v.	Piano sonata no 14, op. 27, no 2 'Mondschein' (mvt 1)	1801
Clementi, M.	Piano sonata, op. 25, no 5 in (mvt 2)	1816
Strauss, R.	Also sprach Zarathustra, Sonnenaufgang , op. 30	1896
Schreker, F.	Irrelohe prelude	1924
Händel, G.F.	Wassermusik, Suite no 2, HWV 349, Alla Hornpipe	1743
Fasch, J. F.	Overture suite, PassepiedI-PassepiedII	1688-1758
Bach, J.S.	Toccata and Fugue, BWV 565	1703-1707
Buxtehude, D.	Toccata, BuxWV 155	1690
Pachelbel, J.	Canon and gigue, canon	1680
Telemann, G.P.	Tafelmusik, Overture suite, overture 1,	1733
Vivaldi, A.	Le Quattro stagioni, La Primavera, op. 8	1725
Biber, H.I. v.	Harmonia artificioso-ariosa , Partita IV, no 7, Polcinello.Presto	1644-1704
Prokofiev, S.S.	Peter and the wolf, march, op. 99	1936
Kodály, Z.	Dances of Galánta	1933
Prokofiev, S.S.	Romeo and Juliet, Monatgues and Capulets, Dance of the Knights	1935
Bartók, B.	The wooden prince, IV, op. 13,	1914-1916
Bizet, G.	Carmen, Habanera	1875
Falla, M.d.	Siete canciones poulares espanolas, no 1	1914
Bach, J.S.	Suite no 3, 'Air', BWV 1068	1718
Fasch, J.F.	Overture suite, 'Air' (mvt 2)	1688-1758
Vivaldi, A.	Le Quattro stagioni, L'Inverno op. 8	1725
Biber, H.I. v.	Fidicinium Sacro-Profanum, sonata 3	1683
Grieg, E.	Peer Gynt , suite no 1, In the hall of the Mountain King, op. 46	1876
Falla, M.d.	El amor brujo, Danza del fin del dia,	1915
Mozart, W.A.	Symphony no 40, mvt 1	1788
Salieri, A.	La Locanderia, Presto overture	1795
Antheil, G.	Ballet méchanique, part 1	1924
Khachaturian, A.	Gayane, The Sabre Dance	1942
Debussy, C.	Suite bergamesque, Clair de Lune (mvt 3)	1890
Ravel, M.	Sonatine 2, movement de menuet	1903-1905
Liszt, F.	Liebestraum no 3, nocturne	1850
Schuman, C.	Piano concert, op. 7(mvt 2)	1833
Chabrier, E.	Habanera	1885
Ravel, M.	Boléro	1928
Mozart, W.A.	Le nozze di Figaro, overture	1786
Salieri, A.	Palmira di Regina, overture	1795
Gershwin, G.	Rhapsody in blue	1924
Copland, A.	The three moods, Jazzy	1921
Mozart, W.A.	Serenata notturna- rondeau no 6, KV 239	1776
Mozart, W.A.	Serenade no 13, Eine kleine Nachtmusik, KV 525	1787

Task 3 (antegrade musical memory) - List of compositions
Part 1.

Composer	Work	Year	Emotion
Giacchino, M.	Ratatouille soundtrack, main theme	2007	peaceful
Sollima, G.	L.B. Files (mvt 1)	2006	scary
Desplat, A.	Chéri soundtrack, The Rose Acacia	2009	sad
Muhly, N.	The Reader soundtrack, Who was She	2008	peaceful
Portman, R.	The Duchess soundtrack, main theme	2008	happy
Rombi, P.	Angel soundtrack, Success	2007	happy
Weihrauch, S.	Elizaveta Bam, scene 8	2007	peaceful
Newman, T.	The good German soundtrack, Unrecht oder Recht	2006	scary
Zimmer, H.	Inception soundtrack, Time	2010	ceremonial
Young, C.	Creation soundtrack, To Emma	2009	sad
Richter, M.	Waltz with Bashir soundtrack, andante/reflection	2008	sad
Powell, J.	How to train your dragon soundtrack, See You tomorrow	2010	happy
Newman, T.	The Good German soundtrack, Kraut Brain Trust,	2006	scary
Sollima, G.	L.B. Files (mvt 2)	2006	peaceful
Schnebel, D.	String quartet, Im Raum (mvt 2)	2006	scary
Adams, J.	Doctor Atomic Symphony (mvt 3)	2007	sad
Tiersen, G. Y.	Tabarly soundtrack, 8 mm	2008	peaceful
Sylvestri, A,	Night at the museum soundtrack, To Washington	2006	ceremonial
Reich, S.	Mallet Quartet, (mvt 1)	2009	happy
Desplat, A.	The curious case of Benjamin Button soundtrack, main theme	2009	peaceful
Desplat, A.	Coco avant Chanel soundtrack, Chez Chanel	2009	happy
Glass, P.	Songs and Poems for Solo Cello, Song 3	2006	sad
Dodd, N.	Treasure Island soundtrack, Main Theme	2006	scary
Zimmer, H.	Da Vinci Code soundtrack, Chevalier de Sangreal	2006	ceremonial
Zimmer, H.	Pirates of the Carrabean, The Brethren Court	2008	scary
Desplat, A.	The Queen soundtrack, Tony and Elizabeth	2006	happy
Bell, J. and Zimmer, H.	Angels and Demons soundtrack, 503	2010	sad
Eastwood, C.	Changeling soundtrack, end theme	2008	peaceful
Gubaidulina, S.	Glorious Percussion (mvt 1)	2008	scary
Giacchino, M.	Up soundtrack, Carl goes up	2009	happy

Part 2

Composer	Work	Year
Powell, J.	How to train your dragon soundtrack, See You tomorrow	2010
Sylvestri, A,	Night at the museum soundtrack, Daley Devices	2006
Shaiman, M.	The Bucket List soundtrack, Hospital Hallway	2007
Reich, S.	Mallet Quartet (mvt 1)	2009
Desplat, A.	Chéri soundtrack, main theme	2009
Sylvestri, A,	Night at the museum soundtrack, To Washington	2006
Giacchino, M.	Ratatouille soundtrack, main theme	2007
Badelt, K.	Pour Elle soundtrack, Lisa and Oscar	2009
Muhly, N.	The Reader soundtrack, Who was She	2008
Young, C.	Creation soundtrack, The Ghost Paravane	2009
Navarrate, J.	Cracks soundtrack, Fiamma's Theme	2009
Desplat, A.	Chéri soundtrack, The Rose Acacia	2009
Doyle, P.	Pars vite et reviens tard soundtrack, Camille	2007
Zimmer, H.	Da Vinci Code soundtrack, Chevalier de Sangreal	2006
Richter, M.	Waltz with Bashir soundtrack, andante/reflection	2008
Marianelli, D.	The soloist, Pershing square	2009
Glass, P.	Violin sonata	2008
Sollima, G.	L.B. Files (mvt 1)	2006
Newman, T.	The Good German soundtrack, Kraut Brain Trust	2006
Muzzey, K.	Palladio, main theme	2008
Djawadi R.	Clash oft the titans soundtrack, There is a Good in You	2010
Zimmer, H.	Inception soundtrack, Time	2010
Tiersen, Y.	Tabarly soundtrack, 8 mm	2008
Desplat, A.	Coco avant Chanel soundtrack, Coco rêve de Paris	2009
Glass, P.	Songs and Poems for Solo Cello, Song 3	2006
Bradshaw, M.	Bright Star soundtrack, Yearning	2009
Barsotti, M.	Pope Joan soundtrack, main theme	2010
Bell, J., Zimmer, H.	Angels and Demons soundtrack, 503	2010
Desplat, A.	The curious case of Benjamin Button soundtrack, main theme	2009
Newman, T.	Little Children, Tissue	2006
Rombi, P.	Angel soundtrack, Success	2007
Hooper, N.	Harry Potter and the Half-Blood Prince soundtrack, Living Death	2009
Zimmer, H.	Sherlock Holmes soundtrack, Catatonic	2010
Schnebel, D.	String quartet, Im Raum (mvt 2)	2006

Weihrauch, S.	Elizaveta Bam, scene 15	2007
Weihrauch, S.	Elizaveta Bam, scene 8	2007
Sollima, G.	L.B. Files (mvt 2)	2006
Pärt, A.	Los Angeles, Symphony No. 4 (mvt 3)	2008
Glass, P.	The American Four Seasons, 2nd Violin concerto, (mvt 2)	2009
Desplat, A.	Coco avant Chanel soundtrack, Chez Chanel	2009
Zanelli, G.	Honour soundtrack, theme from The pacific	2009
Giacchino, M.	Up soundtrack, Carl goes up	2009
Newman, T.	The good German soundtrack, Unrecht oder Recht	2006
Barsotti, M.	Pope Joan soundtrack, Pope Joan Suite	2010
Barsotti, M.	Pope Joan soundtrack, Letter in the Forrest	2010
Portman, R.	The Duchess soundtrack, main theme	2008
Howard, J. N.	I am legend soundtrack, My Name is Robert Neville	2007
Gubaidulina, S.	Glorious Percussion (mvt 1)	2008
Young, C.	Creation soundtrack, To Emma	2009
Desplat, A.	Twilight Saga, New Moon soundtrack, main theme	2009
Desplat, A.	Harry Potter and the deathly Hallows soundtrack, The Deathly Hallows	2007
Dodd, N.	Treasure Island soundtrack, main Theme	2006
Adams, J.	Doctor Atomic Symphony (mvt 3)	2007
Dodd, N.	The Imaginarium of Dr. Parnassus soundtrack, Suicide Attempt	2008
Eastwood, C.	Changeling soundtrack, end theme	2008
Narrate, J.	El laberinto del fauno soundtrack, Lullaby	2006
Adams, J.	A Flowering tree, act 1, scene 1	2006
Zimmer, H.	Pirates of the Carrabean soundtrack, The Brethren Court	2008
Howard, J. N.	The Last Airbender soundtrack, Flow like Water	2010
Desplat, A.	The Queen soundtrack, Tony and Elizabeth	2006

Object memory task

Sixteen cards of the Modern Art Memory Game (© 2011 www.ammobooks.com) depicting stylized animals were successively shown for 20 sec. Subjects were asked to name the two most prominent colors. In an incidental memory task 90 minutes later, the same cards were shown together with cards depicting similar animals. Subjects were asked to select the card that was previously shown.

Face memory task

Twenty pairs of b/w pictures of male faces were presented. Subjects were asked to study the faces for 20 sec. In an incidental memory task 90 minutes later, one of the faces was presented together with a similar looking face. Subjects were asked to select the previously encountered face.

Statistical analysis

Statistical analyses were performed using Bayesian inferential tests developed for comparison of an individual with a control sample and a Bayesian test for dissociations in single case studies [S3].

Statistical comparison of PM and control subgroups in musical memory tasks

PM vs. expert musicians[1]

- task 1: $p = 0.47$
- task 2: $p < 0.0001$
- task 3: $p = 0.32$

PM vs. amateur musicians[1]

- task 1: $p = 0.69$
- task 2: $p = 0.25$
- task 3: $p = 0.61$

Amateur vs. expert musicians[2]

- task 1: $p = 0.1$
- task 2: $p = 0.008$
- task 3: $p = 0.04$

[1] - Bayesian inferential tests developed for comparison of an individual with a control sample

[2] - Mann Whitney test

Copyrights / Permissions Figure 1.

F. Mendelssohn Bartholdy	Stadtgeschichtliches Museum Leipzig www.stadtgeschichtliches-museum-leipzig.de
Max Richter	Paul Tingen, www.tingen.org
Muzio Clementi	Verlag Dohr Köln, www.dohr.de
Ludwig van Beethoven	Beethoven-Haus Bonn, www.beethoven-haus-bonn.de
Giovanni Sollima	Rita Antonioli, www.aerreimage.com
Arvo Pärt	Kaupo Kikkas, www.kaupokikkas.com

Supplemental References

S1. Härting, C., Markowitsch, H., Neufeld, H., Calabrese, P., Deisinger, K., and Kessler, J. (2000). Wechsler Gedächtnistest-Revidierte Fassung (Bern: Huber).

S2. Peretz, I., Champod, A.S., and Hyde, K. (2003). Varieties of musical disorders. The Montreal Battery of Evaluation of Amusia. Ann. N. Y. Acad. Sci. *999*, 58-75.

S3. Crawford, J.R., and Garthwaite, P.H. (2007). Comparison of a single case to a control or normative sample in neuropsychology: development of a Bayesian approach. Cogn. Neuropsychol. *24*, 343-72.

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

8. Publikationsliste

1. Preservation of musical memory in an amnesic professional cellist.
   Finke C*, **Esfahani NE***, Ploner CJ.; Curr Biol. 2012 Aug 7;22(15)

2. Lesion Etiology determines memory performance following hippocampal dammage: a comparative study between hypoxia, herpes encephalitis, temporal neoplastic resections- work in progress
   Esfahani-Bayerl N, Finke C, Braun M, Ostendorf F, Düzel E, Heekeren HR, Hasper D, Storm C, Ploner CJ

3. Posterpresentetion
   Preservation of musical memory in an amnesic professional cellist.
   Society for Neuroscience Washington 2011

4. Posterpresentation
   Lesion Etiology determines memory performance following hippocampal dammage
   Society for Neuroscience San Diego 2013

9. Danksagung

Ich möchte insbesondere herzlich meinem Doktorvater Herrn Prof. Dr. C. J. Ploner danken für die hervorragende Betreuung, all die wertvolle konstruktive Kritik, sowie die anregenden wissenschaftlichen Diskussionen mit ausgezeichneten Ratschlägen, unvergleichlichem Erfahrungsschatz und die insgesamt exzellenten Bedingungen für Forschung und Promotion.
Ich bekam die Möglichkeit die Grundlagen des wissenschaftlichen Denkens und Arbeitens zu erlernen. Ich bin mit einem Thema und Fachbereich vertraut geworden, welches in mir nachhaltig Interesse geweckt hat und welchem ich mich auch in meinem weiteren klinischen sowie wissenschaftlichen Werdegang mit Begeisterung widmen werde.

Weiterhin gilt ein großer und entscheidender Dank Herrn PD Dr. med. Carsten Finke für die hervorragende wissenschaftliche Betreuung und die über Jahre hinweg regelmäßige engmaschige Ansprechbarkeit und vertrauensvolle Zusammenarbeit. Die Arbeit wäre ohne seine Ratschläge, Denkanstöße und Motivation in der Form nicht möglich gewesen.

Ebenso möchte ich herzlich PD Dr. med. Florian Ostendorf und Dr. med. Mischa Braun für die wertvolle wissenschaftliche Unterstützung und ständige und regelmäßige Hilfsbereitschaft danken.
Schließlich gilt ein großer Dank den interessierten Probanden, insbesondere den Berliner Philharmonikern, welche auch kurzfristig für lange, mühevolle Termine und Versuchsreihen zu gewinnen waren und sehr hilfsbereit und unermüdlich zur Verfügung standen.
Schließlich geht ein Herzensdank an meine Familie für ihren bedingungslosen Glauben, die liebevolle Unterstützung und ständige Motivation für meinen Weg.