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### UNIVERSITY FOR MUSIC, DRAMA AND MEDIA HANNOVER Institute of Music Physiology and Musicians' Medicine

## Absolute pitch ability, cognitive style and autistic traits: a neuropsychological and electrophysiological study

### THESIS

Submitted in partial fulfillment of the requirements for the degree of Doctor of Natural Sciences

### Doctor rerum naturalium (Dr. rer. nat.)

awarded by the University of Veterinary Medicine Hannover

by

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Hannover, 2019

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Date of final exam: 25th October, 2019

Parts of the thesis have been published previously in:

- Wenhart, T., Hwang, Y. & Altenmüller, E. (2019). *Enhanced auditory disembedding in an interleaved melody recognition test is associated with absolute pitch ability.* **Scientific Reports**. DOI: http://dx.doi.org/10.1038/s41598-019-44297-x
- Wenhart, T. & Altenmüller, E. (2019). A tendency towards details? Inconsistent results on auditory and visual local-to-global processing in absolute pitch musicians. Frontiers in Psychology. DOI: http://dx.doi.org/10.3389/fpsyg. 2019.00031
- Wenhart, T., Bethlehem, R.A.I., Baron-Cohen, S. & Altenmüller, E. (2019). Autistic traits, resting-state connectivity and absolute pitch in professional musicians: shared and distinct neural features. **Molecular Autism**. DOI: http://dx.doi.org/10. 1186/s13229-019-0272-6

### Sponsorship:

Teresa Wenhart received a PhD scholarship by the German National Academic Foundation (Studienstiftung des deutschen Volkes)

To my parents,

to my family and friends,

to the music

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## List of Abbreviations

AGLT	Auditory Global-Local Test
AMMA	Advanced Measures of Music Audiation
ANOVA	Analysis of Variances
AP	Absolute Pitch (possessor)
AQ	Autism Spectrum Quotient
ASC	Autism Spectrum Condition(s)
EC	eyes closed resting state
EEG	Electroencephalography
EO	eyes open resting state
ERP	Event related potential
GEFT	Group Embedded Figures Test
HL	Hierarchical Letters
ICA	Independent Component Analysis
IFG	Inferior Frontal Gyrus
IFOF	Inferior Frontal Occipital Fasciculus
IMRT	Interleaved Melody Recognition Test
IPG	Inferior Parietal Lobe
ISI	Inter Stimulus Interval
ITI	Inter Trial Interval
MMN	Miss match negativity
(f)MRI	(functional) Magnetic Resonance Imaging
(Gold-)MSI	(Goldsmith) Musical-Sophistication-Index
MST	Minimum Spanning Tree
(p)MTG	(posterior) Mediotemporal Gyrus
PAT	Pitch Adjustment Test
PIS	Pitch Identification Screening
dlPFC	dorso-lateral Prefrontal Gyrus
РТ	Planum Temporale
RP	Relative Pitch (possessor)
SPM	Standard Progressive Matrices
ST	Semitone
(p)STG	(posterior) Superior Temporal Gyrus
STS	Superior Temporal Sulcus
WCC	Weak Central Coherence Theory
ZVT	Zahlenverbindungstest (Trail Making Test)

# List of Symbols

С	response bias
$C_i$	Clustering Coefficient of node i
$C^w$	Average Clustering Coefficient of a weighted graph
d'	sensitivity index
F	F-value
G <sub>con</sub>	Performance on Global congruent trials
Ginc	Performance on Global incongruent trials
imag	imaginary component
$L_i$	Characteristic Path Length of node i
$L^w$	Average Path Length of a weighted graph
L <sub>con</sub>	Performance on Local congruent trials
L <sub>inc</sub>	Performance on Local <b>inc</b> ongruent trials
MAD	Mean Absolute Deviation from target tone in cent (100 cent = 1 semitone)
р	p-value
PC	Phase Coherence
r	Pearson correlation coefficient
real	real component
RT	reaction time in s
SACS	Speed Accuracy Composite Score
SDfoM	<b>S</b> tandard <b>D</b> eviation from <b>o</b> wn <b>m</b> ean in cent (100 cent = 1 semitone)
sgn	sign function
$S_{xyt}$	Cross- <b>S</b> pectrum of time series <b>x</b> and <b>y</b> at timepoint <b>t</b>
t	t-value (student t distribution)
wPLI	(weighted) Phase Lag Index

- Global Clustering Coefficient relative to random network  $\gamma$
- effect size eta
- $\eta \lambda$ Average Path length relative to random network
- Small Worldness,  $\frac{\gamma}{\lambda}$  $\sigma$

"Every act of perception, is, to some degree, an act of creation, and every act of memory is to some degree an act of imagination."

Oliver W. Sacks, Musicophilia: Tales of Music and the Brain

### UNIVERSITY OF VETERINARY MEDICINE HANNOVER

### Summary

Center for Systems Neurosciences (CSN) Institute of Music Physiology and Musicians' Medicine (University of Music, Drama and Media Hannover)

> Doctor rerum naturalium (Dr. rer. nat.)

## Absolute pitch ability, cognitive style and autistic traits: a neuropsychological and electrophysiological study

by Teresa WENHART

Absolute pitch (AP) is defined as the rare ability (<1% in the general population) to name or produce a tone without the use of a reference tone. It is much more common among professional musicians and said to depend on both - early music education under the age of 7 and genetic factors. By contrast, relative pitch ability is an also highly trained skill of musicians to analyse and sometimes explicitly name relations of tones (i.e. intervals). Recently, two studies have reported higher autistic personality traits in absolute pitch musicians and several case reports and small sample studies have frequently found absolute pitch among autistic individuals. Furthermore, similarities in brain connectivity were reported in several studies pointing towards a special relation between segregation and integration ability of the brain in these two populations. However, it is still unclear how this co-occurence can be explained and direct comparisons of the populations or investigations of the relation between absolute pitch and autistic traits are missing.

Autism is characterized by a set of neurodevelopmentally caused symptoms mainly affecting social domains. Autistic individuals show problems with social interaction and communication, repetitive behaviours, restrictive interests and hyper- or hyposensitivities of the senses. Several theories of autism try to explain non-social (and sometimes social) symtoms with a tendency for bottom-up processing pathways, enhanced perceptual sensitivity and a focus on details. These theories comprise the *weak central coherence theory* (WCC), the *enhanced perceptual functioning theory* and the *hypersystemizing theory*. The critical period of absolute pitch development overlaps with a period of detail-oriented perception during normal child development. Hence, a detail-oriented "cognitive style", i.e. the predisposition to process incoming sensory information in a certain way, might serve as a common framework.

The present thesis aims at investigating neurocognitive and neurophysiological characteristics of autism in healthy absolute pitch and relative pitch possessors and their relation to autistic traits in the same population. A total of 31 AP and 33 RP professional musicians and music students participated in a huge comprehensive study which contained resting state electroenzephalographic measurements, assessment of autistic symptoms (Autism Spectrum Quotient, Questionnaire) and auditory and visual experiments investigating cognitive style. The analyses resulted in three publications. In general absolute pitch possessors showed higher autistic traits compared to relative pitch possessors replicating the results of recent studies. Publication 1 reports that absolute pitch possessors outperform relative pitch possessors in an interleaved melody recognition test, which serves as an auditory embedded figures test. Visual and auditory embedded figures tests are often used in the autism literature in order to investigate cognitive style. Absolute pitch possessors seem to have an advantage in the test, which points towards enhanced sensory sensitivity for bottom-up details or availability of additional perceptual cues (i.e. pitch label) in these subjects.

Publication 2 reports inconsistent results on auditory and visual hierarchical stimuli experiments. Participants had to respond to hierarchically constructed letters or melodies and either judge characteristics of the detail or the contextual level of the stimuli. In conflicting (incongruent) situations, interference effects of the unattended level were calculated. Analyses revealed inconsistent interference effects selectively appearing for certain types of measurements (reaction times, accuracy, combined score). The significant associations obtained reveal that absolute pitch possessors, when compared to relative pitch possessors, tend to exhibit a more detail-oriented processing with less contextual integration. However, missing effects on related target parameters might be caused by methodological problems related to investigating cognitive style with hierarchical stimuli.

In publication 3 a graph theoretical approach is used to analyse brain connectivity networks (connectivity estimate: weighted phase lag index) of the resting state electroenzephalographic measurements of absolute and relative pitch possessors. Graph theory is especially suited to compare the efficiency of a brain's information processing capability. A normal human brain exhibits an efficient network of highly connected modules (segregation) with few long-distance connections (integration). The analysis shows that absolute pitch possessors are equipped with a widely underconnected brain with reduced integration and segregation as well as reduced interhemispheric connections. Parts of these results were related to autistic traits.

In conclusion, the present thesis extends the literature on absolute pitch and especially the vague relation to autism: the results on neurocognitive and brain network differences partly overlap with the effects observed in autism or are associated with autistic traits in absolute pitch possessors. This is first evidence, that absolute pitch and autism might be related to each other through similarities in cognitive style and brain underconnectivity (integration deficit hypothesis). Inconsistencies within the results further reflect the heterogeneity of absolute pitch as a phenomenon and emphasize the need for subgroup analyses and longitudinal studies in the future.

### TIERÄRZTLICHE HOCHSCHULE HANNOVER

### Zusammenfassung

Zentrum für Systemische Neurowissenschaften (ZSN) Institut für Musikphysiologie und Musikermedizin (Hochschule für Musik, Theater und Medien Hannover)

> Doctor rerum naturalium (Dr. rer. nat.)

### Absolutes Gehör, kognitiver Stil und autistische Persönlichkeitszüge: eine neuropsychologische und elektrophysiologische Studie

### von Teresa WENHART

Das Absolute Gehör ist definiert als die seltene Fähigkeit (<1% in der Bevölkerung), einen Ton ohne Verwendung eines Referenztons zu benennen oder zu erzeugen. Die Prävalenz bei professionellen MusikerInnen ist dabei gegenüber der Allgemeinbevölkerung deutlich erhöht. Nach bisherigem Forschungsstand ist die Entwicklung dieser Gabe vermutlich abhängig sowohl von frühem musikalischem Training vor dem Alter von 7 Jahren, als auch von genetischen Faktoren. Relatives Gehör, die Fähigkeit der meisten MusikerInnen, die Beziehungen von Tönen (d.h. Intervalle und Melodien) zu analysieren und manchmal explizit zu benennen, ist dagegen bei den meisten MusikerInnen vorhanden und trainiert. Kürzlich haben zwei Studien von vermehrten autistische Persönlichkeitsmerkmale bei MusikerInnen mit absolutem Gehör berichtet. Mehrere Fallstudien und Studien mit kleinen Stichproben haben häufiges Vorkommen von absolutem Gehör bei autistischen Personen festgestellt. Darüber hinaus wurde in mehreren Untersuchungen beider Populationen ähnliche Gehirnkonnektivität in Bezug auf Über- und Unterkonnektivität des Gehirns berichtet. Es ist jedoch noch unklar, wie dieses Zusammentreffen erklärt werden kann. Direkte Vergleiche der Populationen oder Untersuchungen des Verhältnisses von absolutem Gehör und Autismus stehen noch aus.

Autismus umfasst eine Reihe von Entwicklungsstörungen, deren Symptome hauptsächlich soziale Bereiche betreffen. Autistische Personen zeigen Probleme mit sozialer Interaktion und Kommunikation, repetitive Verhaltensweisen, restriktive Interessen und Hyper- oder Hyposensitivitäten der Sinne. Verschiedene Theorien des Autismus versuchen, nicht-soziale (und manchmal auch soziale) Symptome mit einer Tendenz zu Bottom-up-Verarbeitungswegen, gesteigerten Wahrnehmungsfähigkeiten und einer Fokussierung auf Details zu erklären. Zu diesen Theorien gehören die Theorie der *schwachen zentralen Kohärenz*, die *Theorie der gesteigerten Wahrnehmungsfunktionen* und die *Theorie des Hypersystematisierens*. Da sich die kritische Periode für die Ausbildung des absoluten Gehörs mit einer Periode der detailorientierten Wahrnehmung während der normalen kindlichen Entwicklung überschneidet, könnte ein detailorientierter "kognitiver Stil", d.h. die Veranlagung, eingehende sensorische Informationen auf eine bestimmte Weise zu verarbeiten, als gemeinsamer Rahmen für die Erklärung der Ähnlichkeiten dienen. Die vorliegende Arbeit hat zum Ziel, neurokognitive und neurophysiologische Eigenschaften von Autismus bei gesunden absolut (AP)- und relativ (RP) hörenden MusikerInnen und die Beziehung dieser Eigenschaften zu autistischen Merkmalen in derselben Population zu untersuchen. Insgesamt nahmen 31 AP- und 33 RP-BerufsmusikerInnen und Musikstudierende an einer umfangreichen Studie teil, bei der elektroenzephalographische Messungen des Ruhezustands des Gehirns, Messungen autistischer Symptome (Autismus Spektrum Quotient, Fragebogen) und auditorische und visuelle Experimente, die den kognitiven Stil untersuchen, durchgeführt wurden. Im Allgemeinen zeigten Absoluthörende mehr autistische Merkmale als Relativhörende, was die Ergebnisse aus vorherigen Studien repliziert.

In Publikation 1 übertrafen die Absoluthörenden Relativhörende in einem Test zur Erkennung verschachtelter Melodien, einer auditiven Version der *Embedded Figures Tests* (Tests mit verschachtelten visuellen oder auditorischen Elementen). Embedded Figures Tests werden in der Autismusliteratur häufig verwendet, um den kognitiven Stil zu untersuchen. Absoluthörende haben in diesem Test offenbar einen Vorteil, der möglicherweise auf eine verbesserte sensorische Empfindlichkeit für Bottom-Up-Details oder die Verfügbarkeit zusätzlicher Wahrnehmungshinweise (z.B. Ton-Label-Assoziationen) bei diesen ProbandInnen zurückzuführen ist.

In den Experimenten der zweite Publikation mussten TeilnehmerInnen auf hierarchisch aufgebaute Buchstaben oder Melodien reagieren und entweder Merkmale der Detail- oder der Kontextebene der Reize beurteilen. In inkongruenten Situationen wurden Interferenzeffekte der unbeachteten auf die beachtete Ebene berechnet. Analysen ergaben inkonsistente Interferenzeffekte, die für bestimmte Arten von Messungen (Reaktionszeiten, Genauigkeit, kombinierte Bewertung) und Modalität (Hören, Sehen) selektiv auftraten. Die beobachteten Effekte legen nahe, dass Absoluthörende im Vergleich zu Relativhörenden tendenziell eine stärker auf Details ausgerichtete Verarbeitung und eine weniger kontextbezogene Integration besitzen. Jedoch könnte das Fehlen ähnlicher Effekte bei vergleichbaren Zielparametern bedingt sein durch Probleme, den kognitiven Stil mit hierarchischen Stimuli zu untersuchen.

In Publikation 3 wurde ein graphentheoretischer Ansatz verwendet, um die Netzwerkstruktur des Gehirns aus Konnektivitätsschätzungen (gewichteter Phasenverzögerungsindex) der elektroenzephalographischen Daten im Ruhezustand von Absolut- und Relativhörenden zu analysieren. Ein typisches menschliches Gehirn weist ein effizientes Netzwerks aus stark in sich vernetzten Modulen (Segregation) und wenige Querverbindungen zwischen diesen Modulen (Integration) auf. In der vorliegenden Studie zeigten Absoluthörenden jedoch gegenüber Relativhörenden weitestgehend reduzierte Integration und Segregation sowie reduzierte interhemisphärische Verbindungen, was für ein Integrationsdefizit ähnlich der Unterkonnektivitäts-Hypothese bei Autismus spricht. Teile der Ergebnisse korrelieren mit autistischen Zügen innerhalb derselben Stichprobe.

Zusammenfassend erweitert die vorliegende Dissertation den Forschungsstand zum absoluten Gehör und insbesondere dessen Beziehung zu Autismus durch Ergebnisse zu neurokognitiven und Hirnnetzwerkunterschieden. Die Ergebnisse decken sich teilweise mit den bei Autismus beobachteten Effekten oder korrelieren mit autistischen Merkmalen bei Absoluthörenden. Dies ist der erste Hinweis darauf, dass absolutes Gehör und Autismus durch Ähnlichkeiten im kognitiven Stil und in der Konnektivität des Gehirns in Verbindung stehen könnten. Die Inkonsistenzen der Ergebnisse spiegeln darüber hinaus die Heterogenität des absoluten Gehörs als Phänomen wider und unterstreichen die Notwendigkeit für Analysen von Subgruppen von Absoluthörenden sowie für Längsschnittuntersuchungen.

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### Chapter 1

## Introduction

Absolute Pitch has been a matter of scientific interest for over 100 years [1] and even in the general population it receives constant attention as for its fascinating appearance. For non-absolute pitch possessors it seems hardly understandable, why someone can easily name a musical tone or in extreme cases even natural sounds and noises without looking into the sheet music or using any tonal reference. The phenomenon therefore receives similar admiration as other unexplainable special abilities, e.g. eidetic memory or hypercalculation. This often glamourizes absolute pitch possessors with the status of a genius.

### **1.1 Absolute Pitch**

### 1.1.1 Definition and Prevalence

The ability to name or produce a musical tone without the use of a reference tone (hence the term 'absolute'), e.g. the tone of a tuning fork or a comparative tone of a musical instrument, is called *absolute pitch ability* or short *absolute pitch* [1, 2]. If, for example, two tones with a distance of 4 semitones (ST) to each other are presented audially, relative pitch possessors (RP's, i.e. trained musicians without absolute pitch) are able to judge the pitch distance (relation of pitch height (Hz)) between tones, while absolute pitch possessors (AP's) can additionally name the single tones as belonging to a musical tone category (pitch chroma, e.g. "C" or, "F", see Figure 1.1). Furthermore, while RP's would judge the interval independently of the underlying single tones (purple vs. red indicated intervals in Figure 1.1) as "major thirds", AP's also distinguish between different thirds, e.g. a major third between "C" and "E" (purple) and a third between "F" and "A" (red). Some AP's might, however, not be able to state in which octave (C,  $C^2$ ,  $C^3$  etc.) the interval is played (see Figure 1.1 for explanation). Relative Pitch is a very common and usually explicitly trained ability among professional musicians with variable proficiency. In contrary, only very few musicians exhibit absolute pitch ability.

While the phenomenon is rare in the general population (<1%, [1, 4, 5]), it is, however, much more common among musically trained people and especially professional musicians. Prevalence estimations for professional musicians range from 7.6% [6], 12.2% [4] and 15% [7] up to 24.6% at some institutions [6]. Furthermore, the prevalence seems to be higher in populations of Asian ethnic background [4, 6, 8, 9]. It is still under debate, whether the ethnicity effect is due to the influence of tonal mother tongue on the acquisition of absolute pitch early in life [8, 9] or due to differences in musical education methods [4].

Finally, exceptional absolute pitch abilities found in case reports and small sample



FIGURE 1.1: Explanation of absolute versus relative pitch strategies. RP's judge pitches of tones relative to other tones, i.e. they compare the difference in pitch height (= intervals; purple, red). AP's perceive an additional quality: pitch chroma, i.e. the according to music theory verbally labeled categories ("C" -> "H") of single tones [3]. RP's would judge the aurally presented intervals (purple vs. red) independently of the underlying tones as "major thirds"; AP's might as well be able to judge the intervals as major thirds, but also distinguish between different thirds, e.g. a major third between "C" and "E" (purple) and a third between "F" and "A" (red).

studies suggest higher prevalence of absolute pitch in special populations, e.g. congenitally blind persons [10, 11], Williams syndrome [12, 13] and autism [14–19]. The latter will be of major topic within this thesis.

### 1.1.2 Phenomenology

Looking closer onto the ability of naming or producing pitches absolutely, the ability seems far less "perfect" than its appearance. Not only there is inter-individual variability in the proficiency of absolute pitch possessors (e.g. [20]), also the individual performance depends on key [20–22], timbre [22, 23], musical activity [24] and age [21]. Often subjects perform better on white compared to black keys [20, 21, 24] and perceive tones higher than they actually are, which leads to undershooting in adjustment tests and ratings of one or two semitones too high in naming tests [21, 24]. The tendency for a mistuned absolute pitch template increases with increase of age and when musical activity declines [21, 24]. A high rate of octave errors indicating no differences in octave identification between APs and RPs (see [1] for a review) is also often reported. This stresses the view that absolute pitch possessors additionally and dominantly perceive pitch chroma while relative pitch possessors rely on pitch height comparisons in the judgments of tones [22]. Furthermore, the internal template of tone-label associations of absolute pitch possessors can in the short term be distorted by listening to mistuned pieces of music [25]. Usually absolute pitch possessors with higher accuracy are also faster in pitch naming tests [20].

Many absolute pitch possessors report having problems to sing or play in tune or to play the correct notes, when it is required to transpose a melody or piece of music or to play in historic tune. Therefore absolute pitch possessors might lack the ability of singing respectively playing based on intervals (relative pitch) instead of based on absolute pitch cues. Absolute pitch possessors indeed performed weaker in interval labelling if the first note of the interval was mistuned [26]. The same is true for melody comparison (in terms of sameness of intervals), if the melodies are transposed into different tonalities [27]. However, when intervals are not in unusual tuning, absolute pitch possessors outperform relative pitch possessors independent of timbre, key or if a tonal context was given before [28]. These findings suggest, that absolute pitch possessors rely on pitch chroma and the corresponding pitch labels in pitch interval judgments and can outperform relative pitch possessors with this additional cue. If, instead, intervals or melodies are presented in unusual appearance (e.g. differing tuning), interval recognition might be hampered, because tone-label associations are weak or irritating.

### 1.1.3 Acquisition - Genes versus Environment

Most studies suggest that absolute pitch possessors start musical training early in life and on average before the age of 7 years [4, 6, 8, 9, 29]. While explicit training of absolute pitch ability seems to be possible in children at the age of 3-6 years [30–33], to date no study has succeeded to train adults in identifying or producing tones absolutely [32]. Furthermore, some studies also found latent absolute pitch ability in children of ages 3 to 12 years independent of prior musical training [34, 35] suggesting a relation of absolute pitch perception and developmental phase. However, latent AP abilities have also been reported in adults [36, 37]. Many authors in favor of the so called *early learning theory* argue, that the age effect speaks for a *sensitive period* for absolute pitch [7, 33, 38–41], during which sensory learning of tones and

tone names is required to develop or retain absolute pitch ability. There are mainly two positions with respect to the sensitive period aspect:

First, the sensitive period for absolute pitch temporarily overlaps with the sensitive period for speech development [8, 9, 42]. Therefore the development of absolute pitch ability might be critically bound to speech development and learning of speech-tone labels during this period. This is also often used as an explanation for the higher prevalence of absolute pitch among musicians with Asian ethnic background as they have tonal mother tongues [9].



FIGURE 1.2: Influences on the acquisition of Absolute Pitch. If and to what extent an individuum exhibits absolute pitch ability depends on various factors indicated with arrows.

Second, the *perceptual shift theory* stresses that the age span for the development of absolute pitch belongs to a developmental phase (see section "From details to context - developmental shift") during which children exhibit a tendency towards feature based perception [1, 31, 40, 41, 43]. Around the age of 6 to 7 years a developmental shift from a feature-based processing to a more holistic, integrative and relative processing of incoming information happens [39, 40, 43] and the development of absolute pitch becomes less likely or even impossible [1, 43, 44]. For this reason, infants at the age of 8 months use absolute pitch information in a statistical learning paradigm of tone sequences, while adults with and without musical training preliminary solve the same task with the help of relative pitch [39, 40, 42].

Regardless which of the viewpoints one favors, early musical training before age 7 does not always lead to the development of absolute pitch [7]. Rather, a genetic predisposition seems to be necessary as well ([6, 7, 45], see Figure 1.2 for an overview over influences on the acquisition of AP).

Furthermore, with respect to the above mentioned appearance of absolute pitch ability in autism and Williams syndrome (see section 1.2), studies among both developmental conditions have suggested a less important role of age of onset of musical training in the acquisition of absolute pitch ability in these populations [12, 14]. Even if the comparable small samples do not allow for precise estimations of average age of onset or prevalence in these conditions, the extremely good pitch naming abilities and late onset of musical training of the reported cases strengthen the view of a relation between absolute pitch and the genetical and neurodevelopmental aspects of these disabilities. Compared to neurotypical absolute pitch possessors, the sensitive period for development of absolute pitch might be prolonged [12, 14]. Interestingly, a substance which might be at risk of causing autism during pregnancy, valproate, has been shown to enable adults to acquire absolute pitch later in live and therefore might reopen the sensitive period for absolute pitch [46].

In conclusion, absolute pitch ability seems to be an excellent model to research the interaction of genes and environmental influences (as e.g. learning) on the acquisition of cognitive-perceptual abilities and their neural fundamentals [47].

### 1.1.4 Neurocognitive frameworks of absolute pitch ability

Within the neuroscientific and psychological community it has been a matter of debate at which of the stages of the auditory pathway in the nervous system absolute pitch possessors differ from relative pitch possessors. The current chapter will shortly introduce the basic features of the auditory pathway from input of sounds (inner ear) to perception (neocortex). The current state of the neuroscientific and neurocognitive literature will then be summarized and evaluated with respect to the most famous theory of absolute pitch - *the two component theory* [47].

#### Auditory processing in the human brain

Beginning at the outer ear the auditory stimulus travels through the ear channel into the middle ear, where the sound wave is amplified by the three auditory ossicles malleus, incus and stapes. Stapes transduces the resonance onto the oval window, which results in a periodic movement of the liquids and the basilar membrane in the cochlea. The outer and inner hear cells of the basilar membrane within the cochlea are then tonotopically stimulated by the resonance wave and the movement of basilar membrane and (passively) tectorial membrane. This process transforms the periodic sound pressure information via mechanical transformation into electrical signals. From this step on, the auditory stimulus is transmitted via the auditory nerve to the brain stem and further to the subcortical and cortical regions of the brain. At the level of the brainstem, basic feature extraction and analysis occur, e.g. sound intensity and periodicity, timbre, interaural differences in runtime of the signal, and auditory reflexes (e.g. startle reflex). The thalamic relay station, the medial geniculate nucleus, serves as an attentional filter system and processes harmonicity of the auditory signal. The signals of the geniculate nucleus are directly transmitted to the emotion centers of the brain (e.g. amygdala, orbifrontal cortex) already at this early processing stage. Detailed analysis of pitch, timbre, intervals, melodies, musical syntax, musical memory and emotional content etc. is provided by projections of the thalamic nuclei to the primary and secondary auditory cortex (AC) as well as further pathways to higher cognitive and multisensory integration areas. Besides these bottom up pathways, top down projections also provide feedback loops from cortical areas to lower cortical, subcortical or even brainstem areas (see e.g. [48–52]).

#### The two component theory of absolute pitch

Perhaps the most famous neurocognitive account of absolute pitch is the *two component theory* [47]. It proposes that two stages comprise absolute pitch: (1) early

(passive) categorical perception or classification of pitches and (2) late pitch labelling respectively an associative memory process.

During the early stage pitches are passively and ultimately perceived as belonging to certain categories, i.e. pitch chroma information of the pitches is retrieved (see Figure 1.1). Labelling of the pitches with the correct verbal names (e.g. "A", "C-sharp") will then follow by comparing the pitch chroma information with an internally stored pitch template. Notably, the labeling process does not necessarily have to be verbal. Imagery or sensorimotor information could (e.g. in musicians who learn music by heart instead of with sheet music) serve as labels or coding strategies [53, 54].

As AP possessors usually do not have to put effort in naming the notes, these processes run automatically. Therefore an active comparison of the target pitch with a memorized pitch, e.g. the tuning note "A" that many musicians know by heart, rather reflects a specific strategy to solve an AP naming task with relative pitch information. In contrast, the pitch label information of AP possessors is available as naturally as most seeing people can name gross categories of colors as e.g. being "red" or "blue (given the person is not color-blind).

With respect to the anatomical representation of the two stages within the auditory pathway most studies have focused on the neocortex. Early psychophysical experiments comparing AP and RP possessors had already revealed no differences in discrimination of pitches [54], an ability, that does not only depend on cortical, but also subcortical levels within the auditory pathway [55, 56]. Further experiments could show that labelling of tones might be the key difference between absolute pitch and relative pitch perception of tones. For example, absolute pitch possessors do only recall tones better than relative pitch possessors, if they can use the label information of the tested tones [54, 57]. If, instead, the tested tones are above 5000 Hz [57] or tones to compare differ in less than one semitone [54], absolute pitch labels are usually not available for AP possessors. Missing the label information AP possessors did not have an advantage in the pitch memory test anymore [54, 57]. With the information from these studies one might favor the idea that differences occur on cortical level and more specific at comparably later stages of the auditory pathway, i.e. higher cortical areas. This is most strongly supported by the fact that speech processing also depends on cortical processes, especially in regions in the left temporal and frontal lobes (see e.g. [58, 59]).

Various studies focussing on the neocortex have provided evidence for and against either the early or the late neurocognitive component or for the joint two component model. These neurophysiological as well as neuroanatomical investigations are summarized within the next sections.

### Neurophysiological evidence - temporal dynamics

By means of *electroencephalography*, brain processes can be monitored with the use of electrodes that measure brain activity of large populations of neurons on the scalp. This method is particularly useful to investigate temporal dynamics of brain processes, as it exhibits an excellent temporal solution. However, in contrast spatial resolution is relatively unprecise. A standard way of investigating brain processes is to average over brain activity of several trials in which stimuli are presented. The characteristic waveforms that arise shortly after the stimulus presentation, the so called *event related potentials* or *components* (ERP), can then be compared between groups. The earlier a waveform occurs after stimulus presentation (e.g. between 50-150ms), the more primitive or basic processes (e.g. attentional mechanisms, basic

sensory processes) are assumed to be involved. On the other side, late components often are interpreted as reflecting more complex cognitive processes, e.g. multisensory integration, memory processes or whatsoever. A huge amount of studies has tried to relate early (e.g. MMN, mismatch negativity, 100-250ms post stimulus) vs. late (e.g. P300, about 300ms post stimulus) ERPs to early vs. late processing stages in AP possessors to evaluate the two component theory (e.g. [60–65], for a review see e.g. [66]).

While initially some studies had revealed differences with respect to early, i.e. encoding related perceptual components [64, 67–69], a range of other investigations recently only found group differences with respect to late cognitive components [61, 63, 70, 71] if any or could not replicate the findings on early components [62, 65]. As a consequence these findings are currently seen as evidence for differences in associative memory processes, reduced workload on tonal working memory or increased multisensory processes (with respect to available codes for pitch classes) in AP possessors. If and to what extend nevertheless neurophysiological differences in early auditory processes exist between AP and RP possessors is currently unsolved.

#### Neuroanatomical evidence - involvement of different brain regions

Brain imaging methods like (*functional*) magnetic resonance imaging ((f)MRI) can be used to unravel structural (grey and white matter) or functional (activation) differences of brain regions. Compared to electroencephalography or similar electrophysiological methods, MRI and fMRI provide high spatial resolution at the expense of lower temporal resolution (in functional measurements). Several studies have therefore made use of (f)MRI and related methods to yield insights into whether AP possessors show differences in the size of auditory or higher cognitive areas in general or higher activation within these areas during passive or active musical tasks [72–87].

In 1995, Schlaug and colleagues started the discussion on brain regional differences in absolute pitch possessors with their seminal paper on increased leftward hemispherical lateralization of the planum temporale (PT), a region posterior to the primary auditory cortex [88]. PT is traditionally associated with language processing and commonly exhibits a left-right asymmetry with bigger size in the left hemisphere in right-handed subjects (see e.g. [58] for speech related hemispheric differences). This is said to result from language specialization of the left hemisphere in right handers [59]. Schlaug and colleagues [88] have interpreted their finding of an exaggerated size difference of the planum temporale between left and right hemisphere in absolute pitch possessors as stemming from an increased PT in the left hemisphere. However, later, several authors have criticized the interpretation of the data and argued that the difference most likely was caused by a decreased size of the right PT [72, 73]. A range of other studies has found structural or functional differences with respect to absolute pitch ability in the right hemisphere [78, 82–84, 89]. However, initially there had been a great interest in the left hemisphere with lots of findings from all neuroscientific domains [74–76, 79–81, 85, 86]. Interestingly, Wengenroth et al. (2014, [83]) could show the involvement of both the right-sided PT and the left "Broca's area" in an AP-dependent brain network detected with fMRI. The authors therefore suggested that AP pitch encoding might take place in the right hemisphere, while pitch labeling is then conducted by the speech processing regions in the left hemisphere [83]. Furthermore, Schneider et al. (2005, [90]) have found evidence that the hemispheric lateralisation (gray matter volume) of the pitch sensitive Heschel's Gyrus is associated with the pitch perception preference of complex tones in professional musicians: individuals decoding preferentially the fundamental pitch showed left-sided asymmetry while individuals with preference for spectral pitch decoding showed right-sided asymmetry [90]. Increasing research has also related this preference to instrumental choice, musical performance style and a "fingerprint" (Schneider & Wengenroth, 2009, [91]) of the auditory cortex (for a review see [91]).

Therefore the discussion of lateralization of the absolute pitch is of huge interest. In general, the left hemisphere is said to process more detail-oriented, speech relevant and temporally fine-tuned information (e.g. rhythm, speech, rapid pitch changes, fundamental frequency), while the right hemisphere is specialized in spectral auditory perception, processing of information in context (e.g. music in general, more contextual information like melodies) and mental rotation (e.g. [90, 92–96], see [58, 91] for a review). For this reason, differences in the left hemisphere have often been attributed to speech or cognition relevant differences of AP possessors (early categorical perception and verbal cognitive mechanisms), while right hemispheric findings speak for perceptual differences, e.g. in pitch encoding, perhaps already appearing at early auditory processing stages (e.g. Wengenroth et al., 2014, [83]).

Many anatomically oriented studies on AP distinguish between differences in primary auditory cortex e.g. in STS (Superior Temporal Sulcus), STG (Superior Temporal Gyrus) and MTG (Medio temporal Gyrus) [76, 78, 79, 82, 83, 85, 86], and secondary and higher cognitive areas, e.g. frontal and parietal regions like dlPFC (dorso-lateral prefrontal cortex), PT (planum temporale), IPL (inferior parietal lobe) and IFG (inferior-frontal gyrus) [79, 81–83, 86–89, 97] both in the left and the right hemisphere. Primary sensory areas of the brain process comparably more basic sensory information, while secondary or multisensory integration areas perform higher cognitive abilities and multisensory integration. This interpretation is again used for or against early or late processing stages of absolute pitch ability. Compared to electrophysiological studies evidence is therefore less clear in favor or against early or late processes with respect to the two-component theory.

### **1.2** Absolute Pitch and Autism

Two studies have revealed eccentric personality traits and heightened autistic traits in absolute pitch possessors [98, 99]. This is an interesting finding since the miraculous appearance of absolute pitch ability can be compared to the genius-like savant abilities [100] often reported in autism spectrum conditions and one of which is absolute pitch [14–18, 101–105]. This chapter introduces the psychopathology of autism and it's most relevant theoretical frameworks and attempts to review the most important shared and distinct neuroscientific and cognitive findings concerning both conditions.

### 1.2.1 Autism Spectrum Conditions

Autism spectrum conditions (ASC) encompass a set of neurodevelopmentally caused difficulties in social cognition and communication, speech and cognitive development, sensory processing and executive functions [106]. Depending on the severity of the cases symptoms already occur before the age of 3 years. While initially the prevalence was estimated at about 4 in 10.000 children [107] the rate has increased to about 1/150 [108] or even more than 1/100 [109, 110]. Some, but not all of the

affected people never develop speech and/or have intellectual disabilities. Key diagnostical symptoms comprise for example difficulties in social cognitive domains like emotion recognition in faces and gestures, perspective taking, the understanding of sarcasm and in "reading between the lines". Autistic people further have difficulties in coping with unexpected change, have narrow and intense special interests, show repetitive behavior and sensory hyper- or hyposensitivities (DSM 5, APA 2013). However, in contrary, some individuals show superior abilities alongside their disabilities: savant skills [100], visuo-spatial abilities [111], rapid mathematical calculation [112–114], calendar calculation [17], extreme memory [115, 116], musical talent [14, 19] or, as mentioned above, absolute pitch ability [14–18, 101–105]. The interindividual heterogeneity of autistic symtoms is further reflected in the unclear contribution and interplay of several genetic factors with respect to the etiology of autism (for a review see [117-121]). This makes it difficult to validly define subtypes or even prototypes of the condition, hence the terms "spectrum" or "syndrome" ranging from mild or even subclinical phenotypes to very severe cases [122]. Autistic symptoms in the general population might therefore also be distributed rather gradually than discrete [122].

### 1.2.2 Theoretical Frameworks of Autism

In 1985, Baron-Cohen and colleagues [123] proposed in their seminal paper the autistic child might lack the so called *theory of mind*. Theory of mind is an abstract concept from the field of developmental psychology that describes the ability of most humans to reason about the intentions and thoughts of other people e.g. perspective taking, predicting actions etc. [124]. This ability is said to develop between the ages of 3 to 6 years and has been investigated in a range of studies (see e.g. [125, 126] for an overview). The *mind-blindness theory* of autism [123] states that autistic people do not develop the implicit and/or explicit ability to create a theory of mind and that this explains the social cognitive and communicative deficits of autism spectrum disorders.

However, since the theory lacks the explanation of non-social symptoms of autism [127–129] and several studies have failed to replicate the theory of mind deficit [130, 131], a range of other theories to explain autism have emerged. The most famous ones are the *weak central coherence account* [127, 132], the *enhanced perceptional functioning theory* [133] and the *Empathizing-Systemizing theory* [128, 134].

The weak central coherence account (WCC) proposes a detail-oriented cognitive style in autism, that is reflected in a superiority of local feature extraction alongside a relatively weak integration of the features into a global form or contextual meaning [127, 132]. The term *cognitive style* has been defined as "(...) *a general, non-conscious preference for processing information in a particular way.*" ([43], [135] cited after [43]). Against the initial version of the theory to date no complete inability of global processing [136] is said to underlie non-social anormalities in autism but rather a bias towards predominant local processing [132]. The enhanced perceptional functioning theory [133, 137] extends the WCC framework by superior low-level perceptual abilities like increased discrimination of sensory stimuli and a dominance of low-level perception over higher cognitive functions. The authors also attempt to explain savant abilities and special skills in autism by means of the enhanced perceptional functioning theory. Finally, the Empathizing-Systemizing theory [128, 134] tries to integrate the findings from social and non-social domains within a two component theory consisting of an empathizing (social cognition deficits, emotion recognition

etc.) and a systemizing (drive to analyze and interest in systems, weak central coherence, enhanced perception, non-social anormalities) domain.

### **1.2.3** Cognitive and neuroscientific comparison

With respect to the above mentioned findings of autistic traits in absolute pitch musicians [98, 99] and absolute pitch in autistic individuals (e.g. [16, 103–105], see sections 1.2, 1.2.1) it is still unclear how this co-occurrence can be explained. As for the perceptual and cognitive nature of absolute pitch (see two component theory, section 1.1.4), the WCC account and the enhanced perceptional functioning account could serve as a common basis. This idea will be outlined in the following sections.

### From details to context - developmental shift and cognitive style

When comparing absolute pitch with autism in the light of the above-mentioned theoretical frameworks it appears intriguingly intuitive to describe absolute pitch as a more detail-oriented perspective on music and sounds compared to relative pitch. Keeping Figure 1.1 in mind, absolute pitch possessors are not only able to describe pitch differences between tones (intervals, relative pitch), but can retrieve pitch class information (pitch chroma) and therefore label single tones in isolation, i.e. without a given tonal context or a reference tone/system (see chapter 1.1.1). So what if absolute pitch possessors exhibit a more detail-oriented cognitive or perceptual style similar as the WCC theory and other frameworks suggest for autism?

Chin [43] has already reviewed evidence for the view of absolute pitch development being restricted to a) a developmental phase earlier than the transition from feature-based to context-based perception (see als section 1.1.3) and b) people with a predisposition for a more detail-oriented cognitive style:

In 1950, Piaget [138] has for the first time described cognitive phases in the development of children. The transition from single feature based to a more integrative view of the world was described by the shift from the *preoperational phase* to the phase of *concrete operations* between ages 7 and 8, or in other words as a transition from unidimensionality, e.g. single tones, small entities (in music), to multidimensionality, e.g. relative pitch, intervals, melodies [139]. Later the timeframe of the phase transition was corrected to 5-7 years by investigations of several authors (e.g. [140, 141]; [142] cited after [43]). The fact that the transition occurs at this age is already strong evidence for the idea that cognitive style respectively the transition from feature-based to context-based perception plays an important role in the acquisition of absolute pitch as for the critical period of AP before the age of 7 (see chapter 1.1.3). Several studies on children have supported this viewpoint [31, 40, 44].

However, since not all people who receive music education before the age of 7 acquire absolute pitch (see section 1.1.3), the question remains, if perhaps a (genetical) predisposition for a more detail-oriented cognitive style during the whole life might be necessary as well. This could also explain the joint occurrence of absolute pitch and autistic symptoms as autism is also explained by detail-oriented perception and cognition (see section 1.2.2). Many studies investigating detail-oriented perception in vision and audition in autism have made use of embedded figures tests [143–147], hierarchically constructed stimuli with local and global levels [148–152] and illusions [148, 153–157] (see Figure 1.3).

In contrast, only one study has attempted to experimentally investigate cognitive style in absolute pitch possessors. Costa-Giomi and colleagues [41] presented absolute pitch and relative pitch musicians and a non-musical control group with a





visual hidden figures test and found significant better performance of absolute pitch possessors on the test compared to both of the other groups, while no difference between relative pitch musicians and non-musicians were observed [41].

The cognitive style theory could be linked to shared brain connectivity and neurodevelopmental mechanisms between phenomena like absolute pitch and autism. Neuroanatomical and neurophysiological similarities of autism and absolute pitch will be reviewed in the following section.

#### Neurophysiological and -anatomical comparison

Brain anatomical studies and post-mortem investigations have revealed microand macrostructural changes in various brain areas associated with autism (see e.g. [159] for a review). In general, especially frontal, parietal and temporal regions show enlargements in autistic individuals ([160, 161] cited after [159]). Strongest differences are often reported within the frontal cortex and also within the cerebellum (see [159]). Furthermore, the neurodevelopmental time course of the amygdala might be altered in autism in terms of an initial overgrowth during childhood followed by a later similar or even decreased size of this subcortical structure [162, 163].

Interestingly, several studies have found unusual rightward asymmetry of the brain associated with autism and especially with language delay in autistic individuals [164]. The authors did among other difference also report reduced leftward asymmetry with respect to auditory and speech related regions: e.g. Heschl's Gyrus, Planum temporale. In light of the discussion of hemispheric differences in absolute pitch (see section 1.1.4), one might hypothesize that these differences could lead to higher incidence of absolute pitch in autistic individuals. This idea would be consistent with findings of right-sided differences reflecting differences in pitch encoding in absolute pitch possessor [83] and smaller right-hemispheric planum temporale in AP [72]. As a consequence, one might again argue for an early cognitive component characterizing absolute pitch ability (see section 1.1.4). Furthermore, frontal anatomical changes in autism have already been associated with generally reduced neurophysiological connectivity and as a consequence reduced integration of information in autistic individuals [165]. If absolute pitch ability was also reflected by a detail-oriented cognitive style (see section 1.2.3), this could explain the frequent occurrence of absolute pitch in autism.

Finally, reduced interhemispheric connections do also stress the idea of underconnectivity and reduced integration in the autistic brain [166]. Recently, this *underconnectivity hypothesis* has been researched with the use of mathematical techniques. The following section will give a very superficial introduction into the methods of this so called *graph theoretical approach* and will compare results on brain network connectivity in autism and absolute pitch.

### **1.2.4** Brain networks and Graph theory

The human brain fulfills all the criteria of a complex system in that it integrates information from various external and internal sources and always generates new, variable behavior and cognition from a largely defined anatomical structure [167]. Based on the given structural connectivity, for example synapses between neurons or fiber bundles between brain areas, nonlinear dynamic behavior of the neurons or neuronal populations results in statistical dependencies (functional connectivity) or causal interactions (effective connectivity).

A promising approach to analyze the structure of brain networks, i.e. the set of
brain connectivity over long and short distances lies in the use of graph-theoretical approaches. Graph theory is a method from mathematics to analyze various kinds of complex systems, e.g. transportation and electrical systems, social networks and biological systems like cells [168]. Modern imaging techniques allow at least an approximation of structural and functional connectivity [167]. These structural, effective, and functional connectivities of the brain can be represented in the form of an abstract network or graph (see Figure 1.4) with their elements as nodes and their connectivities as edges [169].



FIGURE 1.4: **Illustration of Graph theory for brain network analysis.** Electrophysiological activity is reflected in a graph with the nodes representing the electrode positions (FP1-FT7) and the edges representing shared activity (coherence, phase lag information etc.) between the activities of the two electrodes (connectivity network). The number of edges between two nodes gives the *Path length*, i.e. the shortest distance between the nodes and therefore the efficiency of information flow (*integration*) between them (purple). *Clustering coefficient* measures the number of connections (dark green) between the neighbours of a node (green) in relation to the amount of neighbours. This is an estimate for Clustering or Modules of a network, or, in other words, for *segregation*.

Complex systems in various research areas often exhibit remarkably similar behavior at the macroscopic level in that they share organizational principles (such as the famous *small-world principle*) despite significant differences in the details of their elements, and thus the graphs of these networks can be described by the same network parameters [170]. According to Bullmore and Sporns [171] and Sporns [168], the network structure of the brain is characterized by two opposing principles: the tendency to form local subsystems and modules (local segregation) while maintaining global interaction and integration of information between the modules (global integration).

A measure of local segregation is the *Clustering Coefficient*, which specifies the density of connections between the neighbours of a node by the number of connections between the neighbouring nodes relative to the maximum possible number between them. Highly interconnected neighbouring nodes thus form a cluster or module. The average clustering coefficient also provides a measure of the modularity of a network, that is, the ability of the network to have many segregated modules, and thus many connections within those modules but few between them. In contrary, *Characteristic Path Length* reflects global integration within a network by estimating the average shortest paths between pairs of nodes in the network. This corresponds to the number of edges between the two nodes and is a measure of the efficiency of the communication between them, but not necessarily a measure of spatial (anatomical) distance (see e.g. [168, 172, 173] for an overview about graph theory and network parameters).

Perhaps the most prominent finding with respect to neurodevelopmental differences in autism is an early overgrowth of the brain in autistic children, which is later followed by massive axonal pruning and leads to an underconnectivity of the brain in adulthood [166, 174], especially between frontal cortex and other brain regions [175]. The autistic brain exhibits an exaggerated connectivity (hyperconnectivity) within single brain regions, e.g. sensory and frontal areas, alongside reduced interregional connections (hypoconnectivity) throughout the brain, or in other words higher segregation and lower integration [165, 175–183]. Interestingly, studies have revealed similar brain connectivity patterns of hypo- and hyperconnectivities in absolute pitch compared to relative pitch musicians [77, 79, 80].

While brain network connectivity respectively graph theoretical measures have been associated with autistic symptoms in autism and with absolute pitch performance in absolute pitch possessors, it is unclear in how far these factors interact as for the joint occurrence of autistic traits and absolute pitch ability in both populations. Especially, several authors have suggested that a detail-oriented cognitive style could be reflected by the characteristic hyper- and hypoconnected brain structure and thus might be related to both, absolute pitch and autism [17, 43, 101, 165]. However, to the best of my knowledge, up to date no studies investigating this issue have been conducted.

#### 1.3 Aims

This doctoral project aims at investigating the cognitive and neurophysiological underpinnings of a possible relation between absolute pitch ability and autistic traits in absolute and relative pitch professional musicians. In light of the reviewed status quo in this research area, three main targets where set for the project:

- **1. Autistic traits** Standard diagnostical and personality questionnaires will be used to try to replicate the positive relationship between absolute pitch proficiency and autistic traits revealed by [98, 99]. These traits should then be set in relation to the main ideas for this co-occurrence outlined in the introduction: cognitive style and brain networks.
- 2. Cognitive Style Using hierarchically constructed auditory and visual stimuli and auditory embedded figures tests to measure cognitive style it is hypothesized that absolute pitch possessors exhibit a more autism-like bias towards feature based perception and cognition. To make the obtained results comparable to the autism literature it is tried to parallel the experiments as precisely as possible with existing studies among autistic individuals and neurotypical controls.

The general aim is to try to evaluate whether cognitive and perceptual frameworks of autism could serve to explain the co-occurrence.

**3. Brain networks** Brain network similarities of hyper- and hypoconnectivities between absolute pitch and autism have occasionally been reported and used as explanations for co-occurrence of autistic traits and absolute pitch and cognitive style in autism. To unravel whether autistic traits relate to the hypothesized regional hyper- and global hypoconnectivity in absolute pitch possessors resting state electroencephalographic measurements will be collected and analyzed with the use of graph theory.

## Chapter 2

# General Methods, Materials and Statistics

The present chapter will shortly introduce the basic methods underlying all three publications and characterize the sample.

#### 2.1 Participants

Thirty-three relative pitch and thirty-one absolute pitch professional musicians where recruited mainly from the University for Music, Drama and Media via an online survey (https://www.unipark.de). The german wide survey included personality questionnaires, questionnaires regarding musical history and practice time during lifetime and standardized questionnaires with respect to musicality. A pitch identification test with 36 sine tones was used as a screening test for absolute pitch. Professional musicians or music students with location in or near Hannover where invited to participate in two sessions in the lab of the Institute of Music Physiology and Musicians' Medicine. AP and RP groups were created using the online pitch adjustment test and self-reports of the musicians. Main instruments of AP and RP groups where comparable (see Figure 2.1.)

#### 2.2 General Setup

The whole project consisted of a range of questionnaires, cognitive experiments to investigate cognitive style, absolute pitch tests and electroencephalography (see Table 2.1). All experiments (AGLT, HL, IMRT, PAT and EEG recording) were programmed in Python using the toolbox PsychoPy [184, 185]. Statistical analysis was done with the open source statistical package R (https://www.r-project.org/, version 3.5) and network analysis additionally with the toolboxes eeglab [186] and fieldtrip [187] in MATLAB (MATLAB Release 2014a, MathWorks, Inc., Natick, MA, USA). Python, R and MATLAB Code are available at my GitHub repository (https://github.com/TeresaWe/DrThesis). Results of IMRT were published in Scientific Reports (see section 3.1), AGLT and HL in Frontiers of Psychology (see section 3.2), and EEG brain networks in Molecular Autism (see section 3.3). PAT, AQ and control measures (see Table 2.1) where used for all three publications.



FIGURE 2.1: Main instruments of absolute and relative pitch possessors. The diagrams show the percentage of the main musical instruments separately for each group.



FIGURE 2.2: **Group averages of autistic traits.** Absolute pitch possessors show higher autistic traits (Autism-Spectrum-Quotient) on subscale imagination as well as marginally on attention to detail and communication (a) and on total score (b). One point is given for each item mildly or strongly agreeing with a specific autistic trait (maximum: total=50, subscale =10, [188]). Error bars reflect standard errors.

Session	Acronym	Test	Paper
online	MSI	Musical Sophistication Index [189]	1-3
	hours	total hours of musical practice	1-3
	GUF	Geräuschüberempfindlichkeits-Fragebogen	-
	PIS	Pitch Identification Screening	1-3
	E-S	Empathizing-Systemizing Test [190]	-
	AQ	Autism Spectrum Quotient [188]	1-3
	Hand	Edinburgh Handedness Inventory [191]	1-3
	demogr	Demographic questions, comorbidity	1-3
Session 1	AGLT	Auditory Global-Local Test [150]	2
	GEFT	Group Embedded Figures Test [158]	1
	HL	Hierarchical Letters [192]	2
	ZVT	Zahlen-Verbindungs-Test [193]	1-3
	AMMA	Advanced Measures of Music Audiation [194]	1-3
	SPM	Raven's Standard Progressive Matrices [195]	1-3
	IMRT	Interleaved Melody Recognition Test [147, 196]	1
Session 2	PAT	Pitch Adjustment Test (+EEG)	1-3
	EO	EEG Resting State (eyes open)	3
	EC	EEG Resting State (eyes closed)	3

TABLE 2.1: Experiments and Measurements. Used questionnaires, intelligence tests, experiments and electrophysiological measurements are listed in order of the deduction in the sessions. Tests and Questionnaires during the survey appeared in semi-randomized order. Several tests and questionnaires were used as control variables or targets (PAT, AQ) in all publications.

#### 2.3 Autism Spectrum Quotient and Pitch Adjustment Test

The Autism-Spectrum-Quotient [188], consists of 50 items with four answers each and measures autistic traits at five subscales: social interaction, social communication, imagination, attention to detail and attention switching. Absolute pitch possessors, as expected, exhibited higher autistic traits than relative pitch possessors - in general and on subscales (see Figure 2.2 and publications 3.1, 3.2, 3.3).

The Pitch Adjustment Test built after Dohn et al. 2014 [24] was created to measure fine-graded differences in absolute pitch performance. The task for the participants was to aurally adjust a sine wave with a randomly chosen start frequency until it fits to a target note provided visually as musical label on a PC screen. By using a USB-Controller (Griffin PowerMate NA 16029, Griffin Technology, 6001 Oak Canyon, Irvine, CA, USA) participants had the choice between rough (steps of 1/10semitones) or fine (1/100 semitone resolution) tuning of the frequency. The most important advantages of this method are, that it is nearly impossible to use relative pitch strategies because of the randomly chosen frequency in steps of ST/100. Furthermore it allows the precise measurement of the pitch template of the participant. For example, while some AP possessors might be able to tune the sine wave as close as 1/10 of a semitone to the target frequency, others might show higher variability. All subjects adjusted 108 sine waves to the target tones of the 12 pitch classes, each occurring 6 times. For the task 15 seconds maximum time was given. After 15s the test proceeded with the next trials unless a button was pressed earlier by the subject to confirm the current frequency. This lead to trial length ranging from about 3 to 15



FIGURE 2.3: Absolute Pitch (PAT) performance per subject by group (AP vs. RP). AP's deviations were mostly below 100 cent (=1 ST), while RP's deviations remained at around 300 cent (=3 ST's, chance level). red: smoothed median of absolute deviations of 108 trials over time (max. 15 s, max. 160-163 time points) per subject, blue: smoothedgroup median, green = smoothed group mean, black: 95% confidence interval.

seconds. As visible in Figure 2.3 AP subjects on average reached the requested target frequency with deviations below one semitone and already at around 5 seconds (latency mean AP = 5.59s) after onset of the tone. RP's showed much higher deviation over the whole timespan and higher insecurity after 5 seconds (latency mean RP's = 5.80) of adjustment time, even if on average the deviation did not change anymore onwards. In both groups, cases performing in between AP and RP groups are visible (see Figure 2.3). However, the AP-like lines of three RP cases might be due to median estimation from very few trials at the end of the timespan and therefore comprise plotting artefacts.

Absolute pitch possessors outperformed relative pitch musicians on all pitch classes with respect to final deviation to target tone (F (1, 6882) = 31.31, p < 2.29 e-8). A main effect of pitch category (post hoc t-tests not significant after Bonferroni-Holm correction) but no interaction between group and target were found (target: F(17, 6882) = 1.63, p < 0.049; group x target: F(11,6882) = 1.31, p = 0.213), see Figure 2.4). Latency of the first deviation minimum between current frequency and target tone (see Figure 2.5) also significantly differed between groups and target notes (group: F(1, 6881) = 4.94, p < .026; target: F(17, 6881) = 1.95, p < .011; Post hoc t-tests: E < B: p< .008, E < C#: p< .093, Bonferroni-Holm corrected), while no interactions were found (F(11, 6881) = 0.95, p = 0.487). Interestingly, the mean latency between groups only differs by 0.21s. Therefore on average 5 seconds is the time taken by the participant to adjust the sine wave to the imagined target (whether correct or not) and no further improvement happens afterwards.

To answer the raised research questions of the present thesis (see section 1.3) the measurements of autistic traits (Autism-Spectrum-Quotient, AQ) and pitch adjustment test (PAT) introduced in this chapter were set in relation to experiments on cognitive style in vision and audition as well as to brain network connectivity. This work is summarized in three publications within the following Chapter **??**. Further methodical and statistical details about AQ and PAT are provided in each publication as well.



FIGURE 2.4: **Absolute deviation from target tone** Means and confidence intervals (95%) of average absolute deviations from target tone by group (green=RP, blue=AP) and pitch class. AP's significantly outperformed RP's on all pitch categories. Confidence was also higher in AP respectively variance lower. The main effect of target note did not reach significant post-hoc t-tests (Bonferroni-Holm correction).



FIGURE 2.5: Latency of minimum deviation from target tone. Means and confidence intervals (95%) for latency plotted by group (green=RP, blue=AP) and pitch class. AP's reach the minimum deviation significantly earlier than RP's and tone categories differed significantly in latency across groups. A main effect of target note but no interaction of target and group were found. Only the differences between E and B and (marginally) E and C# remained significant after Bonferroni-Holm correction of post-hoc t-tests.

## Chapter 3

## **Publications**

# 3.1 Enhanced auditory disembedding in an interleaved melody recognition test is associated with absolute pitch ability

Teresa Wenhart, Ye-Young Hwang & Eckart Altenmüller (2019)<sup>1</sup>

Wenhart, T., Hwang, Y. & Altenmüller, E. (2019). Enhanced auditory disembedding in an interleaved melody recognition test is associated with absolute pitch ability. Scientific Reports. DOI: http://dx.doi.org/10.1038/s41598-019-44297-x

*Author contributions:* 

Experimental design: TW (80%), EA (20%) Programming of Experiments: TW(40%), Hannes Schmidt(30%), Pablo Carra(15%), Artur Ehle (15%) Conducting the experiments: TW (60%), Fynn Lautenschlänger(35%), YH (5%) Data acquisition and pre-processing, Statistical analysis: TW (80%), YH (20%) Writing of manuscript: TW Contribution to the writing and revision of manuscript: EA, YH.

<sup>&</sup>lt;sup>1</sup>The current chapter corresponds to an article already published in the journal Scientific reports 9, Article number: 7838 (2019)

#### 3.1.1 Abstract

Absolute pitch (AP) and autism have recently been associated with each other. Neurocognitive theories of autism could perhaps explain this co-occurrence. This study investigates whether AP musicians show an advantage in an interleaved melody recognition task (IMRT), an auditory version of an embedded figures test often investigated in autism with respect to the these theories.

A total of N=59 professional musicians (AP=27) participated in the study. In each trial a probe melody was followed by an interleaved sequence. Participants had to indicate as to whether the probe melody was present in the interleaved sequence. Sensitivity index d' and response bias c were calculated according to signal detection theory. Additionally, a pitch adjustment test measuring fine-graded differences in absolute pitch proficiency, the Autism-Spectrum-Quotient and a visual embedded figures test were conducted.

AP outperformed relative pitch (RP) possessors on the overall IMRT and the fully interleaved condition. AP proficiency, visual disembedding and musicality predicted 39.2% of variance in the IMRT. No correlations were found between IMRT and autistic traits.

Results are in line with a detailed-oriented cognitive style and enhanced perceptional functioning of AP musicians similar to that observed in autism.

#### Keywords:

absolute pitch, disembedding, autistic traits, musicians, auditory streaming, cognitive style, enhanced perception

### 3.2 A tendency towards details? Inconsistent results on auditory and visual local-to-global processing in absolute pitch musicians

Teresa Wenhart & Eckart Altenmüller (2019)<sup>2</sup>

Wenhart, T. & Altenmüller, E. (2019). A tendency towards details? Inconsistent results on auditory and visual local-to-global processing in absolute pitch musicians. Frontiers in Psychology. DOI: http://dx.doi.org/10.3389/fpsyg.2019.00031

Author contributions:

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<sup>&</sup>lt;sup>2</sup>The current chapter corresponds to an article already published in the journal Frontiers of Psychologie, 2019, Vol. 10

#### 3.2.1 Abstract

Absolute pitch, the ability to name or produce a musical tone without a reference, is a rare ability which is often related to early musical training and genetic components. However, it remains a matter of debate why absolute pitch is relatively common in autism spectrum disorders and why absolute pitch possessors exhibit higher autistic traits. By definition absolute pitch is an ability that does not require the relation of tones but is based on a lower-level perceptual entity than relative pitch (involving relations between tones, intervals, and melodies).

This study investigated whether a detail-oriented cognitive style, a concept borrowed from the autism literature (weak central coherence theory), might provide a framework to explain this joint occurrence. Two local-to-global experiments in vision (hierarchically constructed letters) and audition (hierarchically constructed melodies) as well as a pitch adjustment test measuring absolute pitch proficiency were conducted in 31 absolute pitch and 33 relative pitch professional musicians.

Analyses revealed inconsistent group differences among reaction time, total of correct trials and speed-accuracy-composite-scores of experimental conditions (local vs. global, and congruent vs. incongruent stimuli). Furthermore, amounts of interference of global form on judgements of local elements and vice versa were calculated. Interestingly, reduced global-to-local interference in audition was associated with greater absolute pitch ability and in vision with higher autistic traits.

Results are partially in line with the idea of a detail-oriented cognitive style in absolute pitch musicians. The inconsistency of the results might be due to limitations of global-to-local paradigms in measuring cognitive style and due to heterogeneity of absolute pitch possessors. In summary, this study provides further evidence for a multifaceted pattern of various and potentially interacting factors on the acquisition of absolute pitch.

#### **Keywords:**

absolute pitch, cognitive style, week central coherence, autistic traits, musicians

# 3.3 Autistic traits, resting-state connectivity and absolute pitch in professional musicians: shared and distinct neural features

Teresa Wenhart, Richard A. I. Bethlehem, Simon Baron-Cohen & Eckart Altenmüller (2019)<sup>3</sup>

Wenhart, T., Bethlehem, R.A.I., Baron-Cohen, S. & Altenmüller, E. (2019). Autistic traits, resting-state connectivity and absolute pitch in professional musicians: shared and distinct neural features. **Molecular Autism**. DOI: http://dx.doi.org/10.1186/s13229-019-0272-6

Author contributions:

Experimental design: TW (80%), EA (20%) Programming of Experiments: TW(40%), Hannes Schmidt(30%), Pablo Carra(15%), Artur Ehle (15%) Conducting the experiments: TW (60%), Fynn Lautenschlänger(35%), Ye-Young Hwang (5%) Data acquisition and pre-processing: TW Network analysis and Statistical analysis: TW (70%), RB (30%) Writing of manuscript: TW Contribution to the writing and revision of manuscript: EA, RB, SB.

<sup>&</sup>lt;sup>3</sup>The current chapter corresponds to an article already published in the journal Molecular Autism, 2019, 10:20

#### 3.3.1 Abstract

#### Background

Recent studies indicate increased autistic traits in musicians with absolute pitch and a higher proportion of absolute pitch in people with autism. Theoretical accounts connect both of these with shared neural principles of local hyper- and global hypoconnectivity, enhanced perceptual functioning and a detail-focused cognitive style. This is the first study to investigate absolute pitch proficiency, autistic traits and brain correlates in the same study.

#### Sample and Methods

Graph theoretical analysis was conducted on resting state (eyes closed and eyes open) EEG connectivity (wPLI, weighted Phase Lag Index) matrices obtained from 31 absolute pitch (AP) and 33 relative pitch (RP) professional musicians. Small Worldness, Global Clustering Coefficient and Average Path length were related to autistic traits, passive (tone identification) and active (pitch adjustment) absolute pitch proficiency and onset of musical training using Welch-two-sample-tests, correlations and general linear models.

#### Results

Analyses revealed increased Path length (delta 2-4 Hz), reduced Clustering (beta 13-18 Hz), reduced Small-Worldness (gamma 30-60 Hz) and increased autistic traits for AP compared to RP. Only Clustering values (beta 13-18 Hz) were predicted by both AP proficiency and autistic traits. Post-hoc single connection permutation tests among raw wPLI matrices in the beta band (13-18 Hz) revealed widely reduced interhemispheric connectivity between bilateral auditory related electrode positions along with higher connectivity between F7-F8 and F8-P9 for AP. Pitch naming ability and Pitch adjustment ability were predicted by Path length, Clustering, autistic traits and onset of musical training (for pitch adjustment) explaining 44% respectively 38% of variance.

#### Conclusions

Results show both shared and distinct neural features between AP and autistic traits. Differences in the beta range were associated with higher autistic traits in the same population. In general, AP musicians exhibit a widely underconnected brain with reduced functional integration and reduced small-world-property during resting state. This might be partly related to autism-specific brain connectivity, while differences in Path length and Small-Worldness reflect other ability-specific influences. This is further evidence for different pathways in the acquisition and development of absolute pitch, likely influenced by both genetic and environmental factors and their interaction.

#### **Keywords:**

absolute pitch, autistic traits, brain networks, graph theory, musicians, electroencephalography

## Chapter 4

# Discussion

The following sections will summarize and discuss the main findings presented in the publications of chapter **??** and provide an outlook towards future research directions.

#### 4.1 Main findings

In section 1.3 three main aims of the present thesis have been introduced. The results of the publications are summarized in order of the research aims.

#### 4.1.1 Autistic traits

With the use of the Autism-Spectrum-Quotient [188] previous results by Dohn et al. (2012, [98]) were replicated showing generally more autistic traits in absolute pitch possessors and specifically on the subscales imagination, communication and attention to detail. This expected result confirms the hypothesis and the aim to search for explanations of a joint occurrence of absolute pitch and autistic traits (see section 1.2).

#### 4.1.2 Cognitive style

Visual and auditory embedded figures tests (Publication 3.1) and hierarchically visual and auditory stimuli (Publication 3.2) were psychophysically presented to absolute and relative pitch possessors.

Interleaved melody recognition test and performance time on a standard embedded figures test from the autism literature [147, 158] provided strong evidence for the hypothesis of a local-perceptual advantage in absolute pitch possessors consistent with Costa-Giomi et al. (2006, [41]). Absolute pitch possessors showed an advantage in recognizing interleaved melodies in general, and especially of fully interleaved melodies. This can be explained by a detail-oriented cognitive style or enhanced perceptual functioning making use of pitch label information. Furthermore, performance on auditory and visual embedded figures tests were correlated pointing towards an association between visual and auditory cognitive style and a general cognitive bias being measured. However, no correlations were obtained between extent of detail-oriented cognitive bias and autistic traits (neither in audition nor in vision). The results are consistent with Bouvet et al. (2013, [147]), who showed an advantage for autistic children in the fully embedded condition. In contrast to autistic children in their study, however, absolute pitch possessors were not impaired in the separation conditions [147].

In contrast, hierarchically local-to-global tests revealed inconsistent results with respect to the influence of absolute pitch and autistic traits on interference of global or local elements on perception of the respective other. Only two selective interference effects of reaction times and accuracy scores in the auditory paradigm were correlated with absolute pitch performance and showed a tendency towards more detail-oriented perception being associated with absolute pitch proficiency. Interestingly, in vision reduced global-to-local interference was associated with higher autistic traits. The failure to yield consistent results across reaction time, accuracy and combined scores for both local-to-global and global-to-local interference pointed towards methodically concerns in the use of hierarchical stimuli to investigate cognitive style. This is consistent with the view of e.g. Kimchi & Palmer (1982, [197]). In summary, the two studies on cognitive style partially confirmed the hypothesis of a tendentially more detail-oriented perception and cognition associated with absolute pitch possessors, consistent with the idea of Chin (2003, [43]). This detailoriented perception and cognition is partially, but not necessarily, bound to higher autistic traits revealed in the same sample.

#### 4.1.3 Brain networks

Finally, electroencephalographic measurements of the resting brain were analyzed using a graph theoretical network approach to quantify segregation and integration capability of the participants' brains (Publication 3.3). Results revealed a generally underconnected brain network of absolute pitch possessors with reduced clustering, reduced integration and reduced small-worldness in beta, delta and gamma bands, respectively. Post-hoc single connection comparisons pointed towards especially reduced interhemispheric connections between temporal electrodes. Interestingly, reduced clustering was also related to higher autistic traits. Brain network measures and autistic traits together explained roughly 38% of pitch adjustment and 44% of variance of pitch naming ability of professional musicians. In general, the results show a brain connectivity endophenotype of absolute pitch possessors partly overlapping with that one observed in autism [165, 166, 178, 179] and reported in previous studies among absolute pitch possessors [77]. Importantly, this is partly even associated with autistic traits in the same absolute pitch possessors. Brain network characteristics therefore argue for an integration-deficit hypothesis of absolute pitch.

#### 4.2 General Discussion

#### 4.2.1 Absolute pitch - a heterogeneous ability

Absolute pitch, the unique ability to be able to name or produce a musical tone without the use of any kind of reference [1] has been said to depend both on genetic factors and on an early sensitive period (see section1.1.3). Specifically it has been acclaimed as

"(...) one of the cleanest examples of a human cognitive ability that arises from the interaction of genetic factors and environmental input during development. In particular, unlike most other cognitive functions (including language and memory, which are influenced by multiple factors and interact with many general brain functions), AP is distributed relatively discretely in the population, and its expression is neatly encapsulated, as it seems unrelated to most other cognitive functions." (Zatorre, Nature Neuroscience, 2003, [47]).

But perhaps absolute pitch is not as clear and "clean" as thought. Other authors, e.g. Wengenroth et al. (2014, [83]), have already argued for a more steadily or even

a uniform distribution of absolute pitch [83]. The present research indicates that autistic traits, cognitive style and brain network connectivity play a role in this ability. But (1) inconsistency of results on cognitive style, (2) the increased, but only in some absolute pitch possessors critically high autistic traits, (3) the missing correlation of cognitive style with autistic traits (4) and the brain network characteristics only partly overlapping with autism speak for a heterogeneous ability. The question if and to what extend a co-occurrence of autistic traits and absolute pitch can be explained by shared cognitive and neuroscientific characteristics might therefore only be answered on subgroup level. Or, in other words, autistic traits, cognitive style and brain network connectivity might be related to absolute pitch (and perhaps to each other) only within a subgroup of absolute pitch possessors. However, in the present study, subgroup analysis was not possible because of restrictions with respect to sample size.

Nevertheless, the present work shows, that an integrative view of several influencing factors and characteristics of the ability (see Figure 4.1) alongside a brain network perspective is necessary to get more insight into the specific relations between brain, special ability and disability.



FIGURE 4.1: Update: Influences on the acquisition of Absolute Pitch. If and to what extend an individuum exhibits absolute pitch ability relates to various factors indicated with arrows. As a results of the present studies cognitive style and autistic traits are also important. Interrelation of influencing factors (e.g. autistic traits and brain network) not shown.

#### 4.2.2 Absolute pitch and autism - a common framework?

The question whether the weak central coherence account [132], the enhanced perceptional functioning theory [133, 137] or other cognitive theories of autism can explain the co-occurrence of autistic traits and absolute pitch cannot finally be resolved in this thesis. Rather it seems that autistic traits and the perceptual-cognitive characteristics only comprise one among a range of other influencing factors (see section 4.1). While enhanced auditory disembedding (Publication 3.1), and the tendency towards a more detail-oriented processing of auditory and visual hierarchical stimuli (Publication 3.2) speak for enhanced perceptual functioning respectively weak central coherence, the inconsistency of the results and the only partially occurring correlations with autistic traits weaken the interpretation.

Based on the results from network analysis (Publication 3.3) it is hypothesized, that both shared and distinct features of autism and absolute pitch exist. Perhaps, while in general, early musical training during a cognitively sensitive period is important for the acquisition of absolute pitch (see section 1.2.3), in a subgroup of AP's, a lifelong tendency for detail-oriented information processing (Publications 3.1, 3.2) and a less integrative brain network (Publication 3.3) might increase the likelihood to develop absolute pitch ability - even later in life [14, 46]. The interrelation or even a causal relation of brain connectivity, genetic factors and cognitive style, however, has yet to be explained. Nevertheless, a predisposition for detail-oriented processing or less integrative brain connectivity might explain the on average and individually (often subclinically) higher autistic traits in absolute pitch possessors and the higher incidence of absolute pitch in autism. Therefore, the onset of music exposition might be of less importance in those populations, consistent with the results of Gervain et al. (2013, [46]) and Heaton et al. (1998, [14]).

In conclusion, this might lead to subgroups of absolute pitch possessors that are distinguished by either a more genetically (neurocognitive predisposition) or a more experience based etiology of absolute pitch. However, studies relating genetic influences in the acquisition of absolute pitch to cognitive style, brain network features and autistic traits are missing as are subgroup analyses with much higher sample sizes.

#### 4.2.3 Strengths and Limitations

Several limitations of the studies have to be discussed:

First, no autistic and neurotypical musically matched control groups were included. A direct comparison with cognitive, neurophysiological and personality traits of autistic people might have helped to understand the differences between relative and absolute pitch possessors. Initially there was indeed a plan to include the two subgroups, but the effort failed due to problems to recrute and motivate autistic individuals to participate in such a long study with several appointments in the lab. Furthermore, the 10 autistic subjects that could be measured showed a high heterogeneity of musical experience and comorbid disorders. Therefore an even higher sampled size would have been required to account for all of these covariables. Especially, four of the autistic participants already reported to have absolute pitch ability. Second, as the present study is a cross-sectional study, no interpretations can be made on the acquisition and development of absolute pitch. Also, the hypothetical interpretation of possibly existing subgroups within the population of absolute pitch possessors can only be proven by subgroup analyses on bigger sample sizes.

Third, no correlation analyses between results from cognitive experiments and brain

network analysis were performed. This could have helped to get an insight into the interrelation between them. This was mainly due to the inconsistency of cognitive results (Publication 3.2) and of the relation of cognitive results to autistic traits (Publication 3.1).

Nevertheless, the project has for the first time investigated cognitive style, autistic traits and brain networks in the same subjects with absolute and relative pitch abilities. Especially with respect to the dimension of the study (one hour survey, 4 hours lab) the sample size of N=64 subjects including the 31 comparably rare absolute pitch possessors is a big strength of the study.

#### 4.2.4 Future directions

Apart from the already mentioned necessity to analyze larger populations of absolute pitch possessors towards existing subgroups, it would be worth to conduct longitudinal studies on neurotypical children in the future. This would help to disentangle the influence of genetic, personality and experience based factors on the acquisition of absolute pitch and on cognitive style and brain networks. Furthermore, genome-based studies, which are up to date missing in absolute pitch possessors, could be included. This would in turn have implications for music education and education of children in general, if, as expected, some exhibit genetically predispositions towards a different view of the world. Whether one does or does not see the forest behind the trees could then be accounted for.

#### 4.3 Conclusion

Absolute pitch is a heterogeneous ability and associated with higher autistic traits on average and in some individuals. A tendency towards more feature-based perception and cognition alongside reduced integration in functional resting-state neurophysiologic networks reflect similarities to autism. However, distinct neurophysiological characteristics and influencing factors are also present. In some AP's a predisposition towards a detail-oriented cognitive style, autistic personality traits and an underconnected brain structure might encompass an alternative etiology of absolute pitch that depends less on early exposure to musical training. The question how each human being experiences the world (qualia) is not only of great importance in philosophical discussions, but also to understand clinically and non-clinically groups of special people: autistic people and absolute pitch possessors.

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## Acknowledgements

I would like to express my sincere gratitude and appreciation to my advisor Professor Dr. med Eckart Altenmüller who has been a tremendous mentor for me - both in research and in personal concerns. I would like to thank you for always having and open ear and being reachable by email, for giving me the opportunity to develop my own research ideas and to develop as a scientist and for your personal and support in all issues. Your advice on both research as well as on my career have been priceless. I would also like to thank Professor Dr. Bruno Kopp and Professor Dr. Felix Felmy for their insightful comments and encouragement as my supervision group members. With the help of your advices and critical questions I could widen my research from various perspectives and improve the project. I would further like to thank Michael Großbach and Christos Ioannou for their technical, administrative and especially personal support. Many thanks also go to my student assistances Hannes Schmidt, Artur Ehle, Pablo Carra and my interns, students and volunteers Johanna Brückner, Christina Schneider, Ye-Young Hwang, Fynn Lautenschläger and Samantha Stanton. Not the last I wish to thank all other colleagues at the Institute of Music Physiology and Musicians Medicine - especially to Florian Worschech and Franziska Hodde - for their colleagueships and friendships in the last three years and all the fun we had in the lab. All of you have made this to a fruitful and important time!

My sincere thanks also go to Professor Dr. Simon Baron-Cohen, Dr. Richard A.I. Bethlehem and Dr. Rebecca Kenny who provided me an opportunity to join the Autism Research Center of the University of Cambridge as visiting doctoral student, and who gave access to the laboratory and research facilities. I am very grateful for your supervision in network analysis, Richard, the personal discussions with all of you and the great collaboration among publication of the results. Many thanks also to all other colleagues and my roommates at the ARC and in Cambridge for the intensive period, the pub activities and the warm welcome. I would also like to express my appreciation towards the Studienstiftung des deutschen Volkes for the believe in and the support of my research project, the financial support of the periode abroad and the many possibilities to develop my personality.

A special thanks to my family! Words cannot express how grateful I am to my mother and my father for all of the sacrifices that you've made on my behalf. Without your support of my academic and musical interests this project would not have been possible. Your believe in me and your help in every critical moment was what sustained me thus far. I would also like to thank all of my friends - especially to Julia Kraus, Frederike C. Oertel, Julia Heine and Linda Fischer - who supported me in writing, and incented me to strive towards my goal. I would like express appreciation to my beloved boyfriend Daniel Fricker who always supported me and motivated me to go on in moments when there was no one to answer my queries.

Last but not least I would like to especially thank all participants - students and colleagues from the University for Music, Drama and Media, Hannover and other Music Universities, autistic participants and all other people, that participated in the online surveys - for their patience, their motivation and their interest with respect to the long and enduring experiments and questionnaires. I have enjoyed the many fruitful reports and discussions with lots of you during the course of the experimental sessions and wish you all the best for your musical or otherwise planned future. Without you, this research project would not have been possible!