Special Issue Article

iMedPub Journals
http://www.imedpub.com

JOURNAL OF NEUROLOGY AND NEUROSCIENCE
ISSN 2171-6625

2015
Special Issue

DOI: 10.21767/2171-6625.S10006

Music Intervention, Agitation, Quality of Life and Repetitive Behaviour in People with a Form of Intellectual Disability: A Brief Pilot Report

Artur C Jaschke and Erik JA Scherder

Department of Clinical Neuropsychology, VU University Amsterdam, The Netherlands

Corresponding author: Artur C Jaschke

a.c.jaschke@vu.nl

Departement of Clinical Neuropsychology, Van der Boechorststraat 1, 1081 BT Amsterdam, The Netherlands.

Tel: +31 (0) 6 421 653 00

Citation: Jaschke AC, Scherder EJA. Music Intervention, Agitation, Quality of Life and Repetitive Behaviour in People with a Form of Intellectual Disability: A Brief Pilot Report. J Neurol Neurosci. 2015, S1.

Abstract

Background: Music intervention gains increasing evidence throughout the literature.

Objective: This study investigated to what extent music intervention is applied in a structured way to people with a form of intellectual disability, and whether its application is related to agitation, repetitive behaviour, and quality of life.

Method: Consequently, a survey was administered analysing to what extent music is applied, and whether it is applied in the context of agitation, repetitive behaviour, and quality of life.

Results: A first finding is that clients are exposed to music daily - 2,5 h-3 h of music listening per day - without a specific purpose, i.e. not specifically to reduce e.g. agitation. Furthermore the results show low levels of agitation and repetitive behaviour as well as high quality of life.

Conclusions: Music interventions - passively or actively - remain an important part of a clients' everyday life. Nonetheless, more research is needed to show more compelling and clear results.

Keywords: Music therapy, Music intervention, Intellectual disability, Agitation, Quality of life, Repetitive behavior

Received: June 27, 2015; **Accepted:** August 15, 2015; **Published:** August 17, 2015

Introduction

Evidence of the positive effects of music intervention on cognitive, communicative and social skills in persons with intellectual disabilities (ID) including Autism Spectrum Disorders (ASD) is increasing [1-3]. Music intervention is believed to serve as a "healing force" [4] and is used as a tool to maintain and develop these areas [5-11]. In addition, music intervention appears to have a beneficial influence on brain development, which in turn influences behaviour [12-15].

Challenging behaviour show the highest prevalence according to the World Health Organisation survey 2010 (54%) [16] across the lifespan of people with a form of ID. Behaviours, such as agitation and often also repetitive behaviour within a social context are often difficult to target with therapy [17]. Music, with its calming effects however, approaches these problems from an interactive and yet soothing angle [1,2,17] highlighting the underlying improvement of quality of life for each individual instead of targeting challenging behaviour at the surface of the matter [18].

Agitation is frequently mentioned in the behavioural patterns of people with a form of ID [19,20]. Studies covering this problem however, offer only pharmaceutical solutions, while a generally more riskless solution (read: music intervention) is discarded [2,21].

Against this backdrop, the results of a few studies suggest that interventions, containing music, might improve quality of life and agitation in ID; e.g. Applied Behaviour Therapy [1,22], Social Stories [23], The Nordoff-Robins method [3] and DIR/Floortime [24]. However, these positive effects are mostly based on anecdotal accounts and therefore, these interventions have difficulty to find their way into generally accepted therapeutic approaches [25]. Research investigating therapeutic effects in individuals with an ID, is so far either of an observational or qualitative

nature, complicating firm conclusions [26]. Furthermore, there is a general lack of specified music therapy approaches covering intellectual disabilities alone [26], necessitating further empirical investigation. Nonetheless, several authors have stressed the importance and superiority of music intervention as compared to for example cognitive behaviour therapy [27-29], underlining the beneficial effects of music intervention on reducing agitation and repetitive behaviour, and improving quality of life [27-29].

In line of this argument, it is important to acknowledge the form of music exposure.

On the one hand, passive exposure to music (i.e. listening to music), has shown to have positive influence on behavioral patterns in people with a form of ID, however lacks access to structured therapy strategies [29,30]. On the other hand, the use of organised sounds (read: music) allows synthesising various models of music intervention into basic therapeutic principles and furthermore supports the use of music intervention in clinical practises [31]. Further elaboration on this matter however, will exceed the purpose of this report.

The present report therefore, is meant to investigate and explore three questions: 1) general application and frequency of music intervention and music related exposure in residential community homes for people with a form of ID; 2) the relation between music intervention, quality of life and agitation levels; and 3) structural application of music intervention, if present.

Methods

Population

The population was recruited at residential community homes for persons with an ID in the Netherlands. Participants were selected by a third party, which left the researchers blind to the initial selection process. As this study set out to investigate the structural application of music intervention in first place, a control group setting was not possible. Participants were selected across all life spans regardless of receiving therapy. In the second stage of the investigation, it became apparent who has received a direct form of music therapy and who was only exposed to background music. By removing specific inclusion or exclusion criteria, a wide range of participants could be included into this study, to investigate the above-mentioned research questions. 112 participants returned the surveys, 22 participants had to be excluded, as their surveys were not complete (Response rate 81.4%). The age ranged from 11 to 78 with a mean age of M=42,91 (SD=19,92) with 43 female and 47 male participants. As the majority of family members could not provide the researchers with the exact IQ scores, participants were divided in IQ ranges (< 54 Low functioning; 55 - 84 Mid functioning; > 85 High functioning). The IQ range as well as other significant medical information, was provided by the medical staff at the care home and was obtained from the participants' personal medical files. Seventeen clients were categorised as Low functioning, the majority of 63 under Mid functioning and 10 under High functioning. None of the participating clients was known to have a hearing impairment or a hypersensitivity to acoustic stimuli.

The residential community homes were situated in a more rural area of the Netherlands, where clients, under supervision, are allowed to move around freely. There are no restrictions for the clients in terms of executing their freedom.

Procedure

A Survey was distributed in a major healthcare centre for people with an ID. The survey was administered by the personal care-taker responsible for the residential community houses, where the participants reside. The caregiver, with the client's responses completed the surveys. No further restrictions were given to when and where the survey should be administered. The additional music exposure diary was administered daily over a four week period and was completed by the caregiver based on their observations on client behaviour. These observations concerned the exposure of clients to music, either as background music or active listening by the clients (clients choose and put on music themselves). The used surveys were selected, based on their validity for self-report in people with an intellectual disability.

Informed consent was obtained through family members or representatives in direct interaction with the participants, where possible.

Agitation

To assess the extent of agitation, The Cohen-Mansfield Agitation index (CMAI; [32]) was administered. The CMAI is a 29-point questionnaire with a Likert 1-7 scale, assessing aggressive behaviour from never to multiple times per day. Questions may relate to verbal aggression as well as physical aggression against others and self-harming. The 29 questions are further divided into items such as spitting, cursing, biting, exhibitionism, physical aggression such as hitting, pushing throwing things, excessive screaming, inappropriate laughing or crying, general negativity towards life as well as the misuse of furniture or objects. Additionally, verbal communication was assessed by the use of repetitive and improper sentences and phrases.

Repetitive behaviour

The Repetitive Behaviour Quotient-2, Dutch translation [33], is a 20 point questionnaire, assessing traits of repetitive behaviour in populations with autism and intellectual disabilities. A Likert scale (1-4) determines the scale of repetitive behaviour on points ranging from never to multiple times per day. The scale was developed to give an indication of repetitive behaviour in the context of the clients' surrounding.

Quality of life

Quality of Life of persons with ID was assessed by the Intellectual Disability Quality of Life-16 [34]. This instrument includes 16 questions. These questions are depicted in two drawings presented to the subject (e.g. I, my body, friends) and the action, indicated by the verb (e.g. dancing, working, activities with the family). For a full description of the pictograms used in the IDQOL-16 see [34]. The use of pictures may facilitate the communication with clients, who have difficulties with reading, or understanding verbal information. Answers are recorded with "smileys", which represent a 5-point Likert scale. Again, the use of

pictures enables the client to response to the questions without verbal communication.

Music exposure and music therapy session diary

This diary was developed to get a better insight into the music related activities of the clients. The caretaker completed the diary. The diary was administered over a four week period with focus on the amount of music therapy sessions and music exposure in general. General exposure to music was further subdivided into active (the client puts on music him or herself) or passive listening (the caregiver puts on background music). Furthermore the type of music was recorded in the diary to give an indication of variety in music styles and favourites. Music genres were defined into Radio Charts (top 40), Country, Folk, Pop, Jazz & Funk, Classical, Rock, HipHop & Rap, RnB & Soul and Nursery rhymes (**Figure 1**).

Informed consent was obtained prior to this research from clients, caregivers, family members or legal representatives.

Data Analysis

The received data was computed manually as a sound statistical analysis was not possible due to the unequal division of clients receiving music intervention and clients not receiving such therapy, however were generally exposed to music. Mean and standard deviation scores were computed using a standard sigma formula:

$$M = \frac{\Sigma\, score\ per\ administered\ questionnaire}{\Sigma\, participants}$$

The means were calculated for the three IQ ranges and yielded the here presented scores per IQ domains.

Subsequently, standard deviation was computed using a Sample Standard Deviation formula:

$$s = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}\left(x_i - \bar{x}\right)^2}$$

Level of significance

The significance of the results was manually computed with a standard significance test formula:

$$\frac{\bar{\chi} - \mu_0}{\sigma/\sqrt{\eta}}$$

Results

As there was an unbalanced spread of participants across the expected groups (music therapy N=9 and general exposure to music n=81) a between groups analysis was discarded.

Following results are taken as raw scores without taking music intervention and exposure into consideration.

A Mean score was computed to give an indication of the administered CMAI, RBQ-2 and IDQOL-16.

Music exposure

The music exposure questionnaire has revealed overall exposure to music. Even though clients have not received a form of music therapy, clients regularly listen to music either by turning on the radio themselves or requesting it or by initiative of the caregiver. Analysis of the music exposure diary shows that 56 participants listen passively to music; music is played in the background without the clients requesting it. Twenty-five participants have listened actively to music; choosing the music, requesting it or putting it on themselves. The remaining nine have received a form of music therapy and have furthermore listened actively and passively to music. All three groups are exposed to music 2,5h - 3h on average per day.

Overall level of agitation and perseveration

Scores on the CMAI yielded a relatively low mean (M=45,07; SD 5,94; $p \leq 0,05$) with two outliers: highest score at 102 and lowest 12. However, the average participant scored between 43 and 48 on the Cohen-Manfield Agitation Index.

Overall level of repetitive behaviour

The RBQ-2 also showed a rather low mean of 26,94 (SD 6,23; $p \leq 0,05$), indicating a low level of repetitive behaviour in the tested sample.

Overall quality of Life

The Mean score on the IDQOL-16 was surprisingly high (M=60,33; SD 1,58) with a significance level of $p \leq 0,05$.

Agitation, repetitive behaviour and quality of life and IQ ranges

Splitting the analysis over the individual IQ-ranges revealed no compelling differences. Scores across the low functioning IQ range varied by only few points from the overall mean in the CMAI, RBQ-2 and IDQOL-16 (**Table 1**). Scores in the mid-functioning IQ-range reflect the overall average. This was expected as this group is mostly represented in this sample (**Table 1**).

Here again in-between group analysis was discarded as the here-performed analyses revealed that the samples were divided too unequally to be compared.

Active participation in music therapy

As this study has aimed at analysing the distribution as well as the effect of music intervention in populations with an intellectual disability, the amount of received music intervention was evaluated. Of note however, analysing the amount of participants receiving music therapy, has shown that only nine out of ninety participants do receive a form of music therapy (data not shown).

Discussion

The primary goal of the present study was to examine whether music was applied in a structured way, and whether its application is related to agitation, repetitive behaviour, and quality of life. The administered survey has revealed two interesting developments related to the initial question: 1) music is hardly offered in a structured manner to improve behaviour; 2) agitation and other behavioural problems were very low in the tested sample.

The question arises, if this can be accredited to the passive music exposure, which all clients received. Further research will be needed to find causality between passive music exposure and low levels of agitation.

		week 1							week 2							week 3							week 4						
Date, e.g. 01/08		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
Music Therapy Sessions	0																												
	1																												
	2																												
	>2																												
Length of session	0 in min																												
	1-15																												
	15-30																												
	30-45																												
	> 45																												
Was agressive behaviour present prior to session?	No																												
	Moderate																												
	Strong																												
	Excessive																												
Did agressive behaviour decrease after session?	Yes																												
	No																												
	N/A																												
Active music listening (clients puts on music him/herself)	0 in min																												
	1-30																												
	30-60																												
	60-120																												
	120-180																												
	> 180																												
Was agressive behaviour present prior to active music listening?	No																												
	Moderate																												
	Strong																												
	Excessive																												
Did agressive behaviour decrease after active music listening?	Yes																												
	No																												
	N/A																												
Passive music listening (Music is put on in the background by the caretaker)	0 in min																												
	1-30																												
	30-60																												
	60-120																												
	120-180																												
	> 180																												
Was agressive behaviour present prior to passive music listening?	No																												
	Moderate																												
	Strong																												
	Excessive																												
Did agressive behaviour decrease after passive music listening?	Yes																												
	No																												
	N/A																												
Music listend to	See code																												

Music genre code: "Radio Charts" – RC / Country – CY / Folk – FK / Pop – PP/ Jazz – JZ / Klassiek – KL / Rock – R / HipHop&Rap –HHR / RnB&Soul - RBS / NU- Nurseries

Figure 1 Music exposure and intervention diary (Authors translation). Columns ask, if the client has received music intervention sessions and how often, if yes the length of the session and its influence on possible aggressive behaviour. Furthermore the diary asks, if the client has put on music, music was put on by the caretaker and which genre of music was mainly listened to. This again is related to an increase or reduction in possible aggressive behaviour.

Table 1 Mean scores and SD across the administered survey divided over three IQ ranges recorded in the tested sample.

	RBQ -2	CMAI	IDQOL-16
Low N= 17	M 27,68 (SD 2,89)	M 48,29 (SD 2,01)	M 58,33 (SD 1,99)
Mid N= 63	M 23,73 (SD 3,11)	M 42,11 (SD 3,36)	M 63,81 (SD 4,32)
High N= 10	M 22,16 (SD 2,73)	M 45,44 (SD 2,37)	M 65,20 (SD 2,98)

Table 2 Average age across the divided groups receiving music intervention and not receiving music intervention.

Gender	MT	Mean Age
Male	No N= 40	40,10
	Yes N= 7	50,86
Female	No N= 41	43,73
	Yes N= 2	54,50

Table 3 Mean and individual scores on the manually compared performances on the administered questionnaires. (MT = Music Therapy).

		RBQ-2	CMAI	IDQOL-16
Low	MT N= 1	Score 27	Score 53	Score 56
	no MT N= 16	M 26,73 (SD 3,01)	M 48,01 (SD 2,21)	M 58,12 (SD 4,88)
Mid	MT N= 7	M 25,29 (SD 1,91)	M 43,43 (SD 2,03)	M 63,44 (SD 1,10)
	no MT N= 56	M 23,20 (SD 3,42)	M 41,34 (SD 3,44)	M 63,01 (SD 5,31)
High	MT N= 1	Score 21	Score 51	Score 64
	no MT N= 9	M 22,81 (SD 2,23)	M 45,09 (SD 2,28)	M 65,11 (SD 3,03)

There were no clear differences between the individual IQ ranges in the main sample (no direct/active music intervention group) on test scores on agitation levels, repetitive behaviour and quality of life; constant exposure to either active or passive listening to music might be an indicator - however not solely - for the overall high quality of life and low agitation.

Throughout the literature, music intervention is administered in cases of high agitation levels with the aim to counteract aggressive behaviour [25]. Likewise, Koseki and colleagues have shown that an enriched environment with diverse high levels of activity has a significant effect on the development of young mice, decreasing their agitation levels in adulthood [35]: music can be seen as one of these high level enriched environment activities [35]. In the here presented sample, however, the results do not show a 'direct' need to counteract aggressive behaviour with explicit music therapy, as clients have shown very low scores on agitation and are furthermore exposed daily to music with an average time of 2,5 hours to 3 hours. Nonetheless, there were nine clients who received direct music therapy in addition to the general music exposure (data not shown). A preliminary analysis of this group however, has shown no difference as compared with clients who did not receive direct music therapy on the test scores, which makes a detailed description of the applied intervention optional. Giving the low N in the music therapy group, further investigation as well as a direct comparison was discarded for the purpose of this report.

Clients as well as caregivers recorded an interestingly high score on the administered IDQOL-16. This reflects an overall satisfaction with the facilities and surrounding the clients are living in. This finding can however, not be accredited to the general use of music alone in these facilities.

Finally, no evidence of a clear therapeutic line was evident when analysing application and needs of music intervention in a structural way within the tested sample. The here presented study has recruited the sample with the primary goal of investigating the use of the above-mentioned structural way of music intervention in first place. In the second stage of the analysis, it became apparent, which clients received direct music therapy, making an in-between group analysis not possible (data not shown).

Further research is needed as to how to explain the relation between general music exposure, direct music therapy and levels of agitation, repetitive behaviour and quality of life. Equal distribution across the participating experimental and control groups (a pre - post measurement setting) would make a direct comparison of structured music intervention against no music intervention (read: therapy) possible (**Table 2**). Taking into account the heterogeneity of the participating population, a randomised controlled trial is questionable as the best research methodology, and either an N=1 or block randomisation should be taken into consideration.

This study has hardly embarked on the long journey of how music interventions are administered in practice. Missing therapeutic lines and mistrust towards the benefits of music therapy on behaviour, agitation and quality of life make this form of intervention difficult to administer in a structured way (**Table 3**).

After all, understanding any beneficial form of intervention supports the intention of any therapy: client well-being.

Acknowledgements

With special thanks to 's Heeren Loo (major healthcare centre for people with an intellectual disability) for supporting this research.

References

1 Martin LK (2013) Applied Behavior Analysis: introduction and Practical Application in Music Therapy for Young Children with Autism Spectrum Disorders. In: Kern P, Humpal M (eds.) Early Childhood Therapy and Autism Spectrum Disorders: Developing Potential in Young Children and their Families, London and Philadelphia: Jessica Kingsley publishers 101-116.

2 MacDonald R, Kreutz G, Mitchel L (2012) Music, Health and Wellbeing, Oxford and New York: Oxford University Press.

3 Guerrero N, Turry A (2013) Nordoff-Robbins Music Therapy: An Expressive Dynamic Approach for Young Children on the Autism Spectrum. In: Kern P, Humpal M (eds.), Early Childhood Therapy and Autism Spectrum Disorders: Developing Potential in Young Children and their Families, London and Philadelphia: Jessica Kingsley publishers 130-144.

4 Feder E, Feder B (1981) The Expressive Arts Therapies: Art, Music and Dance as Psychotherapy, Prentice Hall, Englewood Cliffs NJ.

5 Saperston B (1973) The use of music in establishing communication with an autistic mentally retarded child. Journal of Music Therapy 46-54.

6 Nordoff P, Robbins C (1976) Creative Music Therapy. John Day, New York, NY.

7 Bunt L (1978) The Hammersmith Project. A report of a project funded by the National Medical Research Fund, Department of Paediatrics, Charing Cross Hospital Medical School, London.

8 Mundy P, Sigman M, Ungerer J, Sherman T (1986) Defining the social deficits of autism: the contribution of non-verbal communication measures. J Child Psychol Psychiatry 27: 657-669.

9 Humpal M (1991) The effects of an integrated early childhood music programme on social inter-action among children and their typical peers. Journal of Music Therapy 28: 161-177.

10 Thaut MH (1987) Visual versus auditory (musical) stimulus preferences in autistic children: a pilot study. J Autism Dev Disord 17: 425-432.

11 Duffy B, Fuller R (2000) Role of Music Therapy in Social Skills Development in Children with Moderate Intellectual Disability, Journal of Applied Research in Intellectual Disabilities 13: 77-89.

12 Sparks R, Deck J (1986) Melodic intonation therapy. In: Chapey R (ed.) Language Intervention Strategies in Adult Aphasia. 320-332. Williams & Wilkins, Baltimore, MD.

13 Aldridge D, Gustorff D, Hannich HJ (1990) Where am I? Music therapy applied to coma patients. J R Soc Med 83: 345-346.

14 Wan CY, Schlaug G (2010) Music making as a tool for promoting brain plasticity across the life span. Neuroscientist 16: 566-577.

15 Jaschke AC, Eggermont LH, Honing H, Scherder EJ (2013) Music education and its effect on intellectual abilities in children: a systematic review. Rev Neurosci 24: 665-675.

16 World Health Organisation (2010) Prevalence of Intellectual Disabilities and its meaning, WHO Publishing

17 Marley LS (1984) The use of music with hospitalized infants and toddlers: a descriptive study. J Music Ther 21: 126-132.

18 Magee WL, Davidson JW (2002) The effect of music therapy on mood states in neurological patients: a pilot study. J Music Ther 39: 20-29.

19 Ruedrich S, Swales TP, Fossaceca C, Toliver J, Rutkowski A (1999) Effect of divalproex sodium on aggression and self-injurious behaviour in adults with intellectual disability: a retrospective review. J Intellect Disabil Res 43: 105-111.

20 Tyrer P, Oliver-Africano PC, Ahmed Z, Bouras N, Cooray S, et al. (2008) Risperidone, haloperidol and placebo in the treatment of aggressive challenging behavior in patients with intellectual disability: a randomized controlled trial, Lancet 371: 57-63.

21 Jaschke AC (2014) Music intervention as system: reversing hyper systemising in autism spectrum disorders to the comprehension of music as intervention. Med Hypotheses 82: 40-48.

22 Lim HA, Draper E (2011) The effects of music therapy incorporated with applied behavior analysis verbal behavior approach for children with autism spectrum disorders. J Music Ther 48: 532-550.

23 Brownell MD, Arbor A (2013) Social StoriesTM: Pairing the story to Music. In: Kern P, Humpal M (eds.) Early Childhood Therapy and Autism Spectrum Disorders: Developing Potential in Young Children and their Families, London and Philadelphia: Jessica Kingsley publishers 117-129.

24 Carpente JA (2013) DIR®/FloortimeTM Model: Introduction and Considerations for Improvisational Music Therapy. In: Kern P, Humpal M (eds.) Early Childhood Therapy and Autism Spectrum Disorders: Developing Potential in Young Children and their Families, London and Philadelphia: Jessica Kingsley publishers 145-163.

25 Ageranioti-Bélanger S, Brunet S, D'Anjou G, Tellier G, Boivin J, et al. (2012) Behaviour disorders in children with an intellectual disability. Paediatr Child Health 17: 84-88.

26 Concato J, Shah N, Horwitz RI (2000) Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 342: 1887-1892.

27 Sinha Y, Silove N, Hayen A, Williams K (2011) Auditory integration training and other sound therapies for autism spectrum disorders (ASD). Cochrane Database Syst Rev: CD003681.

28 Gold C, Wigram T, Elefant C (2010) Music therapy for autistic spectrum disorder (review). Cochrane Lib 2010: 1 -21.

29 James R (2015) Music therapy for individuals with autism spectrum disorder: a systematic review, Review Journal of Autism and Developmental Disorders 2: 39-54.

30 Jaschke AC (2014) Music intervention as system: reversing hyper systemising in autism spectrum disorders to the comprehension of music as intervention. Med Hypotheses 82: 40-48.

31 Bruscia KE (1987) Improvisational Models of Music Therapy, Charles C Thomas, Springfield, IL.

32 Cohen-Mansfield J, Marx MS, Rosenthal AS (1989) A description of agitation in a nursing home. J Gerontol 44: M77-84.

33 Leekam S, Tandos J, McConachie H, Meins E, Parkinson K, et al. (2007) Repetitive Behaviour Questionnaire -2, Journal of Developmental & Behavioral Pediatrics, 31: 223-229.

34 Hoekman J, Douma JCH, Kersten MCO, Schuurman MIM, Koopman HM (2001) IDQOL - Intellectual Disability Quality of Life. De

ontwikkeling van een instrument ter bepaling van de 'kwaliteit van bestaan' van mensen met een verstandelijke handicap 207- 224.

35 Koseki T, Mouri A, Mamiya T, Aoyama Y, Toriumi K, et al. (2012) Exposure to enriched environments during adolescence prevents abnormal behaviours associated with histone deacetylation in phencyclidine-treated mice, International Journal of Neuropsychopharmacology 15: 1489-1501.

An Original publication of ImedPub in a Special Issue-**Current Trends in Neurodegenerative Diseases and Medical Procedures**, Edited by Dr. Jianqi Cui, Department of Biochemistry and Molecular Biology, School of Basic Medical Sciences, Ningxia Medical University (NXMU), PR China.