

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Supplement

Section I: Literature Search Strategy

Database searched: Scopus

Date of coverage: 2000 to November 2021

Search undertaken: August 2020, September 2020, February 2021, November 2021

((TITLE-ABS-KEY("multiple sclerosis")AND (hearing OR auditory OR "hearing loss" OR "auditory function" OR "hearing dysfunction")) OR (TITLE-ABS-KEY("multiple sclerosis") AND (dizziness OR vestibular OR vertigo OR equilibrium OR balance OR balanced OR "vestibular function"))

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Database searched: Pubmed**Date of coverage: 2000 to November 2021****Search undertaken: August 2020, September 2020, February 2021, November 2021**

(("multiple sclerosis"[MeSH Terms] AND ("auditorially"[All Fields] OR "auditory"[All Fields] OR ("hearing"[MeSH Terms] OR "hearing"[All Fields] OR "hearings"[All Fields]) OR "hearing loss"[All Fields] OR "hearing" [All Fields] OR "auditory function"[All Fields])) OR ("multiple sclerosis"[MeSH Terms] AND ("vestibular"[All Fields] OR ("dizziness"[MeSH Terms] OR "dizziness"[All Fields] OR "dizzy"[All Fields] OR "vertigo"[MeSH Terms] OR "vertigo"[All Fields]) OR ("vertigo"[MeSH Terms] OR "vertigo"[All Fields] OR "vertigos"[All Fields] OR "vertigoes"[All Fields]) OR ("equilibrium"[All Fields] OR "equilibriums"[All Fields]) OR ("balance"[All Fields] OR "balanced"[All Fields] OR "balances"[All Fields] OR "balancing"[All Fields]) OR "vestibular function"[All Fields]) AND

Translations

Multiple Sclerosis[MeSH Terms]: "multiple sclerosis"[MeSH Terms]**auditory:** "auditorially"[All Fields] OR "auditory"[All Fields]**hearing:** "hearing"[MeSH Terms] OR "hearing"[All Fields] OR "hearings"[All Fields]**multiple sclerosis[MeSH Terms]:** "multiple sclerosis"[MeSH Terms]**dizziness:** "dizziness"[MeSH Terms] OR "dizziness"[All Fields] OR "dizzy"[All Fields] OR "vertigo"[MeSH Terms] OR "vertigo"[All Fields]**vertigo:** "vertigo"[MeSH Terms] OR "vertigo"[All Fields] OR "vertigos"[All Fields] OR "vertigoes"[All Fields]**equilibrium:** "equilibrium"[All Fields] OR "equilibriums"[All Fields]**balance:** "balance"[All Fields] OR "balanced"[All Fields] OR "balances"[All Fields] OR "balancing"[All Fields]

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Database searched: Web of Science**Date of coverage: 2000 to November 2021****Search undertaken: August 2020, September 2020, February 2021, November 2021**

Databases= WOS, BCI, BIOSIS, CCC, DRCI, DIIDW, KJD, MEDLINE, RSCI, SCIELO,
ZOOREC, Timespan=2000-2021

```
#1 TS=("multiple sclerosis")
#2 TS=(auditory OR audio OR "auditory function" OR "auditory system")
#3 TS=(hear* OR hearing OR "hearing loss")
#4 #2 OR #3
#5 #4 AND #1
#6 TS=(vestibular OR vestibul* OR "vestibular dysfunction" OR "vestibular system")
#7 TS=(vertigo)
#8 TS=(dizzy OR dizziness)
#9 TS=(balance OR balanced OR balances OR balanc*)
#10 #6 OR #7 OR #8 OR #9
#11 #1 AND #10
#12 #5 OR #11 AND
```

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Database searched: NICE**Date of coverage:** 2000 to November 2021**Search undertaken:** August 2020, September 2020, February 2021, November 2021

(("multiple sclerosis") AND (hearing OR auditory OR "hearing loss" OR "auditory function" OR hear* OR "hearing dysfunction")) OR (("multiple sclerosis") AND (dizziness OR vestibular OR vertigo OR equilibrium OR balance OR balanced OR "vestibular function"))

Section II: Assessment of Bias

Table S1: Assessment of Bias for case-control studies according to RoBANS

| Year | Author | Selection of participants | Confounding Variables | Measurement of Exposure | Blinding of the Outcome of the Assessment | Incomplete Outcome of Data | Selective Outcome Reporting |
|------|---|---------------------------|-----------------------|-------------------------|---|----------------------------|-----------------------------|
| 2002 | Japaridze et al. ^[1] | ? | + | + | - | + | + |
| 2002 | Sartucci and Logi ^[2] | + | + | + | - | + | + |
| 2004 | Alpini et al. ^[3] | - | ? | + | - | + | + |
| 2005 | Aidar and Suzuki ^[4] | + | + | + | - | + | - |
| 2007 | Patkó et al. ^[5] | ? | - | + | - | + | + |
| 2008 | Zeigelboim et al. ^[6] | ? | + | + | - | + | + |
| 2009 | Lima et al. ^[7] | ? | ? | + | - | + | + |
| 2010 | Lewis et al. ^[8] | + | + | + | - | + | + |
| 2010 | Matas et al. ^[9] | + | + | + | - | + | + |
| 2012 | Doty et al. ^[10] | - | + | + | - | + | + |
| 2012 | Saberi et al. ^[11] | + | + | + | - | + | + |
| 2013 | Gabelić et al. ^[12] | + | + | + | - | + | + |
| 2013 | Harirchian et al. ^[13] | + | + | + | - | + | + |
| 2014 | Valadbeigi et al. ^[14] | + | + | + | - | + | + |
| 2015 | Pokryszko-Dragan et al. ^[15] | + | + | + | - | + | + |
| 2018 | Doty et al. ^[16] | - | + | + | - | + | + |
| 2018 | Kavasoglu et al. ^[17] | + | ? | + | - | + | + |
| 2018 | Koura et al. ^[18] | + | + | + | - | + | + |
| 2019 | Elbeltagy et al. ^[19] | - | + | + | - | + | + |
| 2021 | Rishiq et al. ^[20] | ? | + | + | - | + | + |
| 2021 | Srinivasan et al. ^[21] | + | + | + | - | + | + |
| 2021 | Elmoazen et al. ^[22] | + | + | + | - | + | + |

Green “+” = low risk of bias, red “-” = high risk of bias, yellow “?” = unclear risk of bias.

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Table S2: Risk of bias assessment of cohort studies by the Newcastle-Ottawa Quality Assessment form for cohort studies.

| Year | Author | Representativeness of exposed cohort | Selection of non-exposed cohort | Ascertainment of exposure | Outcome of interest not present at the beginning | Comparability of cohorts/confounders | Assessment of the outcome | Follow-up Length | Adequacy of follow-up of cohorts | Study quality |
|------|--------------------------------------|--------------------------------------|---------------------------------|---------------------------|--|--------------------------------------|---------------------------|------------------|----------------------------------|---------------|
| 2002 | Versino et al. ^[23] | * | n/a | * | * | n/a | - | n/a | * | ? |
| 2008 | Burina et al. ^[24] | - | n/a | * | n/a | - | - | - | - | ? |
| 2009 | Eleftheriadou et al. ^[25] | * | - | * | * | * | - | * | * | Poor |
| 2010 | Degirmenci et al. ^[26] | * | - | * | * | * | * | * | * | Good |
| 2016 | Kaytancı et al. ^[27] | - | - | * | - | * | - | * | * | Poor |
| 2019 | Di Mauro et al. ^[28] | * | - | * | * | * | - | * | * | Good |

* = low risk of bias, - = high risk of bias, "n/a" = the criteria does not apply to the paper, "?" = unknown quality of the paper due to the presence of "n/a" criteria.

Table S3: Risk of bias assessment of cross-sectional studies by the Newcastle-Ottawa Quality Assessment form which is adapted for cross-sectional studies.

| Year | Author | Representativeness of the sample | Sample Size | Non-respondents | Ascertainment of exposure (risk factor) | Comparability of groups/confounders | Assessment of the outcome | Statistical test | Study quality |
|------|---------------------------------|----------------------------------|-------------|-----------------|---|-------------------------------------|---------------------------|------------------|---------------|
| 2015 | Parsa et al. ^[29] | - | - | - | * | * | - | * | Poor |
| 2020 | Yang and Liu ^[30] | * | - | * | * | * | - | * | Good |
| 2020 | Inojosa et al. ^[31] | * | - | * | * | * | - | * | Good |
| 2020 | Inojosa et al. ^[32] | * | - | * | * | * | - | * | Good |
| 2021 | Delphi et al. ^[33] | - | - | * | * | * | - | * | Good |
| 2021 | Cochrane et al. ^[34] | * | - | * | * | * | - | * | Good |
| 2021 | Cochrane et al. ^[35] | * | - | * | * | * | - | * | Good |

* = low risk of bias, - = high risk of bias.

Section III: Multiple Sclerosis and Auditory Function

Table S4. Characteristics of studies examining the effects of MS on auditory function

| Test Battery | Author (Year) | Study Type | Sample Size | | PwMS Mean Age (years) | PwMS Age range (Years) | % Female | MS Type (sample size) | MS Duration Mean (range) years | Results of PwMS compared to controls / normative data |
|-----------------|--|-----------------|-------------|----------|-------------------------------|--------------------------------|----------------------|--|--|---|
| | | | PwMS | Controls | | | | | | |
| ABR | Japaridze et al. (2002) ^[1] | Case-Control | 40 | 33 | 30.5 | 18-57 | 77.5 | ? | ? | 65% Abnormal |
| | Versino et al. (2002) ^[23] | Cohort | 65 | 18 | 35.5 | 19-61 | ? | ? | ? | 37.5% Abnormal |
| | Burina et al. (2008) ^[24] | Cohort | 60 | NA | 37.2 | ? | 68.3 | RRMS | ? | 95% Abnormal |
| | Eleftheriadou et al. (2009) ^[25] | Cohort | 46 | 40 | 40 | 20-66 | 45.6 | RRMS | 4.6 | 26% Abnormal |
| | Lima et al. (2009) ^[7] | Case-control | 25 | NA | 42.6 (female) 38 (male) | 33-53 (female) 24-56 (male) | 64.0 | RRMS (14), PPMS (8), Unspecified Progressive (3) | ? | 30% Abnormal |
| | Matas et al. (2010) ^[9] | Case-control | 25 | 25 | 34.88 | 25-55 | 76.0 | RRMS | 4.25 (?) | Significantly different |
| | Saberi et al. (2012) ^[11] | Case-control | 60 | 38 | 29.9 | ? | 73.3 | ? | 3.2 (?) | 20% Abnormal |
| | Pokryszko-Dragan et al. (2015) ^[15] | Case-control | 86 | 40 | 39.55 | 19-60 | 72.0 | ? | 8.57 (1-30) | Significantly different |
| | Kaytancı et al. (2016) ^[27] | Cohort | 20 | 20 | 31.3 | ? | 55.0 | ? | ? | Significantly different |
| | Di Mauro et al. (2019) ^[28] | Cohort | 40 | 40 | 37 | 18-50 | 60.0 | RRMS | 0.8 (0.8-2) | No difference |
| | Delphi et al. (2021) ^[33] | Cross-sectional | 25 | 25 | 31.43 | 18-45 | 72.0 | ? | ? | Significantly different |
| | Rishiq et al. (2021) ^[20] | Case-control | 11 | 9 | 49.5 | 34-68 | 72.7 | RRMS (9), PPMS (1), SPMS (1) | 11.9 (2-30) | Significantly different at high click rate |
| PTA | Srinivasan et al. (2021) ^[21] | Case-control | 45 | 45 | 31.77 | 18-50 | 73.3 | RRMS | 6.1 (5.37) | Significantly different and 55.56 % abnormal |
| | Lewis et al. (2010) ^[8] | Case-control | 47 | 49 | 51.4 | 21-65 | 57.7 RRMS, 28.6 SPMS | RRMS (26), SPMS (21) | RRMS: 12.6 (2-43) SPMS: 23.3 (8-50) | Worse thresholds |
| | Doty et al. (2012) ^[10] | Case-control | 73 | 73 | Males: 45.24 Females: 45.6 | ? | 71.2 | RRMS (57), PPMS (3), SPMS (6), Unspecified (7) | Males: 7.36 (?) Females: 7.84 (?) | No significant difference |
| | Saberi et al. (2012) ^[11] | Case-control | 60 | 38 | 29.9 | ? | 73.3 | ? | 3.2 (?) | Worse thresholds in female PwMS |
| | Di Mauro et al. (2019) ^[28] | Cohort | 40 | 40 | 37 | 18-50 | 60.0 | RRMS | 0.8 (0.8-2) | No significant difference |
| TEOAEs & DPOAEs | Srinivasan et al. (2021) ^[21] | Case-control | 45 | 45 | 31.77 | 18-50 | 73.3 | RRMS | 6.1 (5.37) | Significantly different |
| | Saberi et al. (2012) ^[11] | Case-control | 60 | 38 | 29.9 | ? | 73.3 | ? | 3.2 (?) | No significant difference |
| | Kaytancı et al. (2016) ^[27] | Cohort | 20 | 20 | 31.3 | ? | 55.0 | ? | ? | No significant difference |
| | Di Mauro et al. (2019) ^[28] | Cohort | 40 | 40 | 37 | 18-50 | 60.0 | RRMS | 0.8 (0.8-2) | Significantly lower |

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Table S4 continued: Characteristics of studies examining the effects of MS on auditory function

| Test Battery | Author (Year) | Study Type | Sample Size | | PwMS Mean Age (years) | PwMS Age range (Years) | % Female | MS Type (sample size) | MS Duration Mean (range) years | Results of PwMS compared to controls / normative data |
|--------------|--|--------------|-------------|----------|-----------------------|------------------------|----------------------|-----------------------|--|---|
| | | | PwMS | Controls | | | | | | |
| WDS | Lewis et al. (2010) ^[8] | Case-control | 47 | 49 | 51.4 | 21-65 | 57.7 RRMS, 28.6 SPMS | RRMS (26), SPMS (21) | RRMS: 12.6 (2-43) SPMS: 23.3 (8-50) | No significant difference |
| | Valadbeigi et al. (2014) ^[14] | Case-control | 26 | 26 | 28.9 | 18-40 | ? | RRMS | ? | Lower scores PwMS |
| | Elbeltagy et al. (2019) ^[19] | Case-control | 20 | 20 | 37.6 | 30-50 | ? | RRMS | ? | Significantly lower |
| DPST | Valadbeigi et al. (2014) ^[14] | Case-control | 26 | 26 | 28.9 | 18-40 | ? | RRMS | ? | Significantly different |
| GIN | Valadbeigi et al. (2014) ^[14] | Case-control | 26 | 26 | 28.9 | 18-40 | ? | RRMS | ? | Significantly different |
| | Elbeltagy et al. (2019) ^[19] | Case-control | 20 | 20 | 37.6 | 30-50 | ? | RRMS | ? | Significantly different |
| CAEP | Japaridze et al. (2002) ^[1] | Case-Control | 40 | 33 | 30.5 | 18-57 | 77.5 | ? | ? | 30% Abnormal |
| | Matas et al. (2010) ^[9] | Case-control | 25 | 25 | 34.88 | 25-55 | 76.0 | RRMS | 4.25 (?) | 16% Abnormal |

Abbreviations: PTA= Pure Tone Audiometry, ABR= Auditory Brainstem Response, OAE= Oto-acoustic Emissions, TEOAE= Transient Evoked Oto acoustic emission, DPOAE= Distortion Product Oto acoustic Emissions, CAEP= Cortical Auditory Evoked Potentials, SCP= Slow Cortical Potentials, GIN= Gaps in Noise test, WDS= Word Discrimination Scores, DPST= Duration pattern sequence test, MS= Multiple Sclerosis, PwMS = Persons with Multiple Sclerosis, ? = not reported.

Cells shaded in grey represent test results that were abnormal or showed a difference between PwMS and Controls

Extracted Pure Tone Audiometry Thresholds and Auditory Brainstem Response Results

Table S5: Pure Tone Audiometry Thresholds

| Author (Year) | Group | Test Ear | PTA Threshold Per Frequency (Hz) | | | | | | | | | | | | | | |
|--|-----------------|---------------------|----------------------------------|------|-----------|-------|-----------|-------|-----------|-------|-----------|-------|-----------|-------|-----------|-------|-------|
| | | | 125 | | 250 | | 500 | | 1000 | | 2000 | | 4000 | | 8000 | | |
| | | | \bar{x} | SD | \bar{x} | SD | \bar{x} | SD | \bar{x} | SD | \bar{x} | SD | \bar{x} | SD | \bar{x} | SD | |
| Doty et al. (2012) ^[10] | Male PwMS | Average Across Ears | Not Tested | | | 15.87 | 5.39 | 14.05 | 5.94 | 12.52 | 7.43 | 12.79 | 8.97 | 20.03 | 11.71 | 17.02 | 17.26 |
| | Male Controls | | | | | 14.35 | 8.24 | 15.90 | 8.68 | 15.53 | 8.58 | 17.74 | 8.93 | 22.77 | 16.08 | 20.23 | 22.49 |
| | Female PwMS | | | | | 12.85 | 6.88 | 12.49 | 6.50 | 12.05 | 6.59 | 14.62 | 7.19 | 15.65 | 8.97 | 13.28 | 12.38 |
| | Female Controls | | | | | 11.28 | 7.77 | 12.52 | 7.60 | 10.45 | 6.82 | 11.62 | 8.17 | 13.92 | 8.79 | 12.65 | 12.60 |
| Di Mauro et al. (2019) ^[28] | PwMS | Right | 10.30 | 1.60 | 10.10 | 0.08 | 10.10 | 0.08 | 10.40 | 1.10 | 11.10 | 1.70 | 10.80 | 1.80 | 13.00 | 2.60 | |
| | Controls | Right | 10.90 | 1.40 | 10.80 | 1.60 | 11.00 | 1.90 | 10.80 | 2.30 | 11.00 | 1.20 | 11.90 | 2.40 | 13.90 | 2.40 | |
| | PwMS | Left | 10.30 | 1.70 | 10.90 | 1.20 | 10.40 | 1.90 | 10.40 | 1.30 | 10.80 | 1.10 | 11.40 | 1.70 | 12.50 | 2.20 | |
| | Controls | Left | 10.90 | 1.40 | 10.80 | 1.60 | 11.00 | 1.30 | 10.90 | 2.10 | 11.10 | 1.90 | 11.90 | 2.80 | 13.90 | 2.40 | |
| Srinivasan et al. (2021) ^[21] | PwMS | Average Across Ears | Not Tested | | | 12.22 | 6.40 | 13.11 | 5.92 | 13.61 | 5.90 | 12.55 | 7.19 | 13.66 | 8.06 | 16.16 | 9.08 |
| | Controls | | | | | 8.94 | 5.05 | 9.50 | 4.17 | 9.88 | 3.82 | 9.50 | 5.45 | 10.88 | 5.83 | 12.05 | 5.89 |

Abbreviations:

PwMS = Persons with Multiple Sclerosis, PTA = Pure Tone Audiometry, \bar{x} = Mean, SD = Standard Deviation

Table S6: Auditory Brainstem Response Parameters and Results

| Author (Year) | ABR Parameters | | | | | | Test Ear | Peak Latency (ms) | | | | Interpeak Latencies (ms) | | | | Peak Amplitude (µV) | | | |
|---|--------------------------------------|-------|--------------|------|---------------|-------|---------------------------|-------------------|----------|----------|-------|--------------------------|----------|----------|----------|---------------------|----------|----------|----------|
| | Click Polarity - Transducer | PR | PL | Ave. | BP Filter | Group | | I | III | V | I-III | III-V | I-V | I | SD | III | SD | V | SD |
| Lima et al. (2009) ^[7] | Rarefaction - TDH 39 Headphone | 13.10 | 60 dB SL* | 1024 | 100- 3000 | PwMS | Right | 1.50 | 0.16 | 3.63 | 0.30 | 5.56 | 0.40 | 2.13 | 0.22 | 1.93 | 0.31 | 4.06 | 0.33 |
| | | | | | | | Left | 1.53 | 0.20 | 3.63 | 0.30 | 5.64 | 0.43 | 2.10 | 0.31 | 2.01 | 0.29 | 4.11 | 0.39 |
| Matas et al. (2010) ^[9] | Rarefaction - TDH 39 Headphone | 19.90 | 80 dB nHL | 2000 | 100- 3000 | PwMS | Average Across Ears | 1.53 | 0.13 | 3.72 | 0.31 | 5.78 | 0.37 | 2.21 | 0.26 | 2.03 | 0.27 | 4.26 | 0.35 |
| | | | | | | | Controls | 1.53 | 0.07 | 3.57 | 0.09 | 5.50 | 0.45 | 2.04 | 0.06 | 1.98 | 0.08 | 4.03 | 0.06 |
| Pokryszko- Dragan et al. (2015) ^[15] | ? - Earphone unspecified | 20.30 | 65 dB SL* | 200 | 150- 3000 | PwMS | Right | 1.72 | 0.19 | 3.88 | 0.33 | 5.81 | 0.81 | 2.18 | 0.19 | 2.00 | 0.30 | 4.19 | 0.39 |
| | | | | | | | Controls | 1.70 | 0.14 | 3.85 | 0.16 | 5.73 | 0.23 | 2.14 | 0.12 | 1.87 | 0.18 | 4.02 | 0.20 |
| | | | | | | PwMS | Left | 1.68 | 0.12 | 3.87 | 0.17 | 5.77 | 0.73 | 2.19 | 0.16 | 1.96 | 0.30 | 4.15 | 0.34 |
| | | | | | | | Controls | 1.69 | 0.13 | 3.83 | 0.12 | 5.70 | 0.21 | 2.13 | 0.14 | 1.87 | 0.17 | 4.00 | 0.19 |
| Kaytancı et al. (2016) ^[27] | ? - TDH 39 Headphone | 13.00 | 70 dB nHL | 1500 | 2000- 4000 | PwMS | Right | 2.03 | 0.27 | 4.36 | 0.49 | 6.26 | 0.35 | 2.33 | 0.49 | 1.90 | 0.28 | 4.23 | 0.42 |
| | | | | | | | Controls | 1.45 | 0.30 | 3.52 | 0.31 | 5.38 | 0.53 | 2.07 | 0.44 | 1.85 | 0.48 | 3.92 | 0.53 |
| | | | | | | PwMS | Left | 1.86 | 0.24 | 4.41 | 0.39 | 6.25 | 0.43 | 2.54 | 0.34 | 1.84 | 0.20 | 4.38 | 0.43 |
| | | | | | | | Controls | 1.47 | 0.24 | 3.40 | 0.43 | 5.39 | 0.46 | 1.92 | 0.48 | 1.99 | 0.53 | 3.91 | 0.47 |
| Delphi et al. (2021) ^[33] | Rarefaction - ? | 9.00 | 70 dB nHL | ? | 30- 3000 | PwMS | IA Diff. | ? ? | ? ? | ? ? | 0.40 | 0.46 | 0.35 | 0.24 | 0.49 | 0.46 | 0.40 | 0.48 | ? ? |
| | | | | | | | Controls | ? ? | ? ? | ? ? | 0.15 | 0.12 | 0.34 | 0.35 | 0.27 | 0.30 | 0.19 | 0.16 | ? ? |
| | | | | | | PwMS | Right | 1.89 | 0.11 | 4.25 | 0.14 | 6.32 | 0.13 | 2.30 | 0.11 | 2.21 | 0.09 | 4.48 | 0.13 |
| | | | | | | | Controls | 1.87 | 0.14 | 4.01 | 0.13 | 5.79 | 0.14 | 2.17 | 0.09 | 1.99 | 0.13 | 4.12 | 0.11 |
| Srinivasan et al. (2021) ^[21] | Rarefaction - Insert earphones | 21.10 | 80 dB nHL | 1500 | 100- 3000 | PwMS | Left | 1.80 | 0.15 | 4.30 | 0.15 | 6.19 | 0.14 | 2.29 | 0.08 | 2.19 | 0.14 | 4.51 | 0.11 |
| | | | | | | | Controls | 1.79 | 0.11 | 3.96 | 0.13 | 5.87 | 0.15 | 2.15 | 0.14 | 1.96 | 0.08 | 4.09 | 0.14 |
| | | | | | | PwMS | Average Across Ears | 1.44 | 0.18 | 3.61 | 0.40 | 5.63 | 0.73 | 2.17 | 0.38 | 2.03 | 0.50 | 4.19 | 0.70 |
| | | | | | | | Controls | 1.43 | 0.16 | 3.48 | 0.19 | 5.30 | 0.24 | 2.04 | 0.17 | 1.82 | 0.18 | 3.86 | 0.21 |
| | | | | | | PwMS | Average Across Ears | ? ? | ? ? | ? ? | 6.12 | 0.72 | ? ? | ? ? | ? ? | ? ? | ? ? | ? ? | |
| | | | | | | | Controls | ? ? | ? ? | ? ? | 5.76 | 0.27 | ? ? | ? ? | ? ? | ? ? | ? ? | ? ? | |

Abbreviations:

PR = Presentation Rate, PL = Presentation Level, Ave. = Number of Averages, BP = Band Pass, , x̄ = Mean, SD = Standard Deviation, dB SL = Decibels Sensation Level, dB nHL = Decibels normal Hearing Level, PwMS = Persons with Multiple Sclerosis, IA Diff. = Inter-aural Difference, ? = not reported.

* dB SL reference to hearing thresholds (did not specify hearing thresholds to click or to pure tones)

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Section IV: Multiple Sclerosis and Vestibular Function

Table S7. Characteristics of studies examining the effects of MS on vestibular function

| Test Battery | Author (Year) | Study Type | Sample Size | | Mean Age PwMS (years) | PwMS Age range (Years) | % Female | MS Type (sample size) | MS Duration Mean (range) years | Results of PwMS compared to controls / normative data |
|--------------|---|-----------------|-------------|----------|--|------------------------|----------|-----------------------|--------------------------------|---|
| | | | PwMS | Controls | | | | | | |
| eVEMP | Sartucci & Logi (2002) ^[2] | Case-Control | 15 | 15 | 44.5 | 26-59 | 66.6 | ? | ? | Significantly different |
| | Versino et al. (2002) ^[23] | Cohort | 70 | 18 | 35.5 | 19-61 | ? | ? | ? | 31.4% Abnormal |
| | Alpini et al. (2004) ^[3] | Case-control | 40 | 25 | 38 | 17-71 | 57.5 | ? | ? | 70% Abnormal |
| | Aidar and Suzuki (2005) ^[4] | Case-control | 15 | 15 | 39.3 | ? | ? | ? | ? | Significantly different |
| | Patkó et al. (2007) ^[5] | Case-control | 30 | 30 | 43.4 | 27-60 | 66.6 | ? | ? | Significantly different |
| | Eleftheriadou et al. (2009) ^[25] | Cohort | 46 | 40 | 40 | 20-66 | 45.6 | RRMS | 4.6 (?) | Significantly different |
| | Gabelić et al. (2013) ^[12] | Case control | 30 | 15 | ? | ? | 46.6 | RRMS | 3.93 (0.2-21) | Significantly different |
| | Harirchian et al. (2013) ^[13] | Case-control | 20 | 20 | 30 | 20-40 | 50 | RRMS SPMS | ? | 70% Abnormal |
| | Parsa et al. (2015) ^[29] | Cross-sectional | 34 | 15 | 29.8 | ? | 100 | ? | ? | Significantly different |
| | Kavasoglu et al. (2018) ^[17] | Case-control | 30 | 31 | 30 | 18-45 | 60.0 | ? | < 1 (?) | 23.3% Abnormal No significant difference |
| | Koura and Hussein (2018) ^[18] | Case-control | 20 | 10 | 36.80 | ? | 65.0 | ? | 4.4 (?) | 100% Abnormal |
| | Delphi et al. (2021) ^[33] | Cross-sectional | 25 | 25 | 31.43 | 18-45 | 72.0 | ? | ? | Significantly different |
| | Elmoazen et al. (2021) ^[22] | Case-control | 20 | 10 | Brainstem lesions: 40 No Brainstem lesion: 34.1 | ? | ? | ? | ? | Significantly different |
| oVEMP | Cochrane et al. (2021) ^[34,35] | Cross-sectional | 40 | 20 | 42.4 | 21-55 | 88.0 | RRMS | 9.9 | No significant difference |
| | Gabelić et al. (2013) ^[12] | Case control | 30 | 15 | ? | ? | 46.6 | RRMS | 3.93 (0.2-21) | Significantly different |
| | Parsa et al. (2015) ^[29] | Cross-sectional | 34 | 15 | 29.8 | ? | 100 | ? | ? | Significantly different |
| | Elmoazen et al. (2021) ^[22] | Case-control | 20 | 10 | Brainstem lesions: 40 No Brainstem lesion: 34.1 | ? | ? | ? | ? | Significantly different |
| ENG | Cochrane et al. (2021) ^[34,35] | Cross-sectional | 40 | 20 | 42.4 | 21-55 | 88.0 | RRMS | 9.9 | No significant difference |
| | Zeigelboim et al. (2008) ^[6] | Case-control | 30 | 0 | 42.23 | 27-64 | 80 | RRMS | ? | 86.7% Abnormal |
| | Degirmenci et al. (2010) ^[26] | Cohort | 30 | 30 | 37.9 | 23-56 | 56.7 | RRMS | ? | 90% Abnormal |

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Table S7 continued: Characteristics of studies examining the effects of MS on vestibular function

| <i>Test Battery</i> | <i>Author (Year)</i> | <i>Study Type</i> | <i>Sample Size</i> | | <i>Mean Age PwMS (years)</i> | <i>PwMS Age range (Years)</i> | <i>% Female</i> | <i>MS Type (sample size)</i> | <i>MS Duration Mean (range) years</i> | <i>Results of PwMS compared to controls / normative data</i> |
|-----------------------|---|-------------------|--------------------|-----------------|-------------------------------|-------------------------------|-----------------|------------------------------|---------------------------------------|--|
| | | | <i>PwMS</i> | <i>Controls</i> | | | | | | |
| Dynamic Posturography | Doty et al. (2018) ^[16] | Case-control | 58 | 72 | Males:44.61 Females: 44.60 | ? | 68.9 | ? | Male: 7.03 (?) Female: 6.54 (?) | Significantly different |
| Static Posturography | Inojosa et al. (2020) ^[31,32] | Cross-sectional | 99 | 30 | 35.01 | 18-50 | 68.7 | ? | 5.5 (?) | Significantly different |
| | Yang and Liu (2020) ^[30] | Cross-sectional | 30 | 25 | 50.8 | ? | 76.7 | ? | 14 (?) | Significantly different |
| Rotary Chair | Cochrane et al. (2021) ^[34,35] | Cross-sectional | 40 | 20 | 42.4 | 21-55 | 88.0 | RRMS | 9.9 | Significantly different |

Abbreviations: cVEMP = Cervical Vestibular Evoked Myogenic Potentials, oVEMP = Ocular Vestibular Evoked Myogenic Potentials, MS= Multiple Sclerosis, PwMS = Persons with Multiple Sclerosis, ? = not reported.
Cells shaded in grey represent test results that were abnormal or showed a difference between PwMS and Controls.

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Extracted Vestibular Evoked Myogenic Potentials Results

Table S8: Ocular Vestibular Evoked Myogenic Potentials Parameters and Results

| Author (Year) | Stimulus (polarity) - Trasducer | PR (Hz) | PL | Ave. | BP Filter (Hz) | Group | Side | Peak Latency (ms) | | Amplitude (µV) | | | |
|--|--|------------|------------|------|-------------------|------------------------------------|----------------------|-------------------|----------|-----------------|----------|-------|------|
| | | | | | | | | n1 \bar{x} | n1 SD | p1 \bar{x} | p1 SD | | |
| Gabelić et al. (2013) ^[12] | Click (?) - Headphone | 1 | 130 dB SPL | 100 | 5-1000 | PwMS | Average Across sides | 10.30 | ? | 14.90 | ? | 13.10 | ? |
| | | | | | | Controls | | 9.5 | ? | 14 | ? | 13.3 | ? |
| Parsa et al. (2015) ^[29] | 500 Hz Tone Burst (?) - Insert earphones | ? | 95 db nHL | ? | ? | PwMS with infratentorial plaque | Right | 15.67 | 1.32 | 20.59 | 1.65 | 6.61 | 0.88 |
| | | | | | | PwMS without infratentorial plaque | | 12.21 | 1.00 | 16.90 | 1.32 | 6.61 | 0.60 |
| | | | | | | Controls | | 10.2 | 0.48 | 15.1 | 0.87 | 12.77 | 4.12 |
| | | | | | | PwMS with infratentorial plaque | | 15.74 | 1.66 | 21.40 | 2.88 | 6.48 | 0.68 |
| | | | | | | PwMS without infratentorial plaque | Left | 11.78 | 0.89 | 16.92 | 0.82 | 6.82 | 0.75 |
| | | | | | | Controls | | 10.3 | 0.51 | 14.9 | 0.84 | 12.6 | 4.04 |
| Elmoazen et al. (2021) ^[22] | 500 Hz Tone Burst (condensation) -Supra aural headphones | 5 | 95 dB nHL | 150 | 1-1000 | PwMS with Brainstem lesions | Average Across sides | 11.43 | 1.42 | 16.86 | 1.79 | 3.59 | 3.82 |
| | | | | | | PwMS without Brainstem lesions | | 10.58 | 2.50 | 15.81 | 1.42 | 3.22 | 2.00 |
| | | | | | | Controls | | 10.09 | 0.92 | 14.71 | 1.20 | 2.76 | 1.28 |
| Cochrane et al. (2021) ^[34] | Unspecified Tone Burst (?) - earphone unspecified | ? | ? | 100 | ? | PwMS | ? | 8.50 | 1.70 | 12.90 | 2.20 | 5.20 | 3.50 |
| | | | | | | Controls | | 8.40 | 1.50 | 12.30 | 2.10 | 4.70 | 2.50 |

Abbreviations:

PR = Presentation Rate, PL = Presentation Level, Ave. = Number of Averages, BP = Band Pass, , \bar{x} = Mean, SD = Standard Deviation, dB SPL = Decibels Sound Pressure Level, dB nHL = Decibels normal Hearing Level, PwMS = Persons with Multiple Sclerosis, ? = not reported.

Table S9: Cervical Vestibular Evoked Myogenic Potentials Parameters and Results

| Author (Year) | Stimulus (polarity) - Trasducer | PR (Hz) | PL | Ave. | BP Filter (Hz) | Group | Side | Peak Latency (ms) | | Amplitude (μ V) | |
|---|---------------------------------|---------|---|------|----------------|--------------------------------|----------------------|-------------------|------|----------------------|-------|
| | | | | | | | | \bar{x} | SD | \bar{x} | SD |
| Sartucci and Logi (2002) ^[2] | Click (Rarefaction) - Headphone | 3 | 140 dB SPL | 256 | 10-1500 | PwMS | Right | 15.30 | 3.10 | 22.50 | 2.30 |
| | | | | | | Controls | | 12.5 | 0.8 | 21.3 | 1.5 |
| | | | | | | PwMS | Left | 14.00 | 2.30 | 20.80 | 2.30 |
| | | | | | | Controls | | 12.3 | 0.9 | 20.8 | 1.3 |
| Alpini et al. (2004) ^[3] | Click (Rarefaction) - Headphone | 5 | 95 dB nHL + 70 dB SPL contralateral Masking | 400 | ? | PwMS | Right | 14.40 | ? | 22.40 | ? |
| | | | | | | Controls | | 14.90 | ? | 22.50 | ? |
| | | | | | | PwMS | Left | 13.40 | 2.87 | 18.64 | 2.67 |
| | | | | | | Controls | | 11.12 | 1.64 | 15.15 | 2.51 |
| Aidar and Suzuki (2005) ^[4] | Click (Rarefaction) - Headphone | 2 | 95 dB HL | 200 | 20-1000 | PwMS | Right | 13.49 | 1.77 | 17.84 | 1.27 |
| | | | | | | Controls | | 10.76 | 1.59 | 14.86 | 2.85 |
| | | | | | | PwMS | Left | 14.40 | 1.50 | 21.30 | 3.20 |
| | | | | | | Controls | | 12.7 | 1.5 | 21.3 | 3.7 |
| Patkó et al. (2007) ^[5] | Click (Rarefaction) - Headphone | 5 | 133 dB SPL | 250 | 10-1600 | PwMS | Right | 14.8 | 1.5 | 21.2 | 3.2 |
| | | | | | | Controls | | 12.9 | 1.9 | 20.7 | 2.8 |
| | | | | | | PwMS | Left | 15.48 | 1.40 | 23.94 | 1.51 |
| | | | | | | Controls | | 14.56 | 1.20 | 23.25 | 1.42 |
| Eleftheriadou et al. (2009) ^[25] | Click (Rarefaction) - Headphone | 5 | 105 dB HL | 250 | 5-1500 | PwMS with brainstem lesions | Average across sides | 12.67 | 1.1 | 21.66 | 1.11 |
| | | | | | | PwMS without brainstem lesions | | 15.48 | 1.40 | 24.90 | ? |
| | | | | | | Controls | | 14.56 | 1.20 | 22.1 | ? |
| | | | | | | PwMS | Average across sides | 22.20 | 9.30 | 30.02 | 11.20 |
| Gabelić et al. (2013) ^[12] | Click (?) - Headphone | 1 | 130 dB SPL | 100 | 5-1000 | Controls | Right | 14.6 | ? | 1.90 | ? |
| | | | | | | PwMS | | 12.9 | 1.4 | 21.3 | 1.6 |
| | | | | | | Controls | Left | 20.20 | 7.05 | 30.71 | 16.20 |
| | | | | | | PwMS | | 13.1 | 1.9 | 20.6 | 1.9 |
| Harirchian et al. (2013) ^[13] | Click (Rarefaction) - Headphone | 2 | 95 db nHL + 40 dB nHL contralateral Masking | 200 | 10-1000 | Controls | IA Diff. | 2.05 | 8.80 | 0.70 | 10.90 |
| | | | | | | PwMS | | 0.17 | 2.2 | 0.4 | 2.5 |

Gür, Binkhamis, Kluk (2022)

MS & Audio-Vestibular System: Systematic Review

Table S9 Continued: Cervical Vestibular Evoked Myogenic Potentials Parameters and Results

| Author (Year) | Stimulus (polarity) - Trasducer | PR (Hz) | PL | Ave. | BP Filter (Hz) | Group | Side | Peak Latency (ms) | | Amplitude (μV) | |
|---|--|---------|------------|------|----------------------|------------------------------------|----------------------------|-------------------|------|----------------|-------|
| | | | | | | | | \bar{x} | SD | \bar{x} | SD |
| Parsa et al. (2015) ^[29] | 500 Hz Tone Burst (?) -Insert earphones | ? | 95 db nHL | ? | ? | PwMS with infratentorial plaque | Right | 18.75 | 1.81 | 28.15 | 1.43 |
| | | | | | | PwMS without infratentorial plaque | | 17.44 | 1.03 | 26.89 | 1.87 |
| | | | | | | Controls | Left | 15.25 | 0.9 | 24.55 | 1.07 |
| | | | | | | PwMS with infratentorial plaque | | 19.11 | 1.72 | 28.88 | 2.27 |
| | | | | | | PwMS without infratentorial plaque | Controls | 17.21 | 1.05 | 26.87 | 1.36 |
| | | | | | | Controls | | 15.31 | 0.93 | 24.48 | 1.18 |
| Kavasoglu et al. (2017) ^[17] | Click (Rarefaction) - Headphone | 5 | 100 dB nHL | 100 | 10- 1000 | PwMS | Right | 12.90 | 2.10 | 21.20 | 1.78 |
| | | | | | | Controls | | 12 | 0.9 | 20.6 | 1.95 |
| | | | | | | PwMS | Left | 12.90 | 2.20 | 21.40 | 2.10 |
| | | | | | | Controls | | 12.03 | 0.96 | 20.76 | 1.63 |
| Koura and Hussein (2018) ^[18] | 500 Hz Tone Burst (Rarefaction) -TDH 39 Headphones | 5.1 | 95 db HL | 200 | ? | PwMS | Right | 17.14 | 0.71 | 26.82 | 0.84 |
| | | | | | | Controls | | 13.83 | 1.14 | 20.76 | 3.43 |
| | | | | | | PwMS | Left | 17.20 | 0.56 | 27.17 | 0.75 |
| | | | | | | Controls | | 14.43 | 0.70 | 22.3 | 1.725 |
| Delphi et al. (2021) ^[33] | 500 Hz Tone Burst (?) -? | 5.1 | 95 dB nHL | ? | 10- 1200 | PwMS | Right | 18.20 | 1.93 | 27.37 | 2.45 |
| | | | | | | Controls | | 14.96 | 1.02 | 24.21 | 2.10 |
| | | | | | | PwMS | Left | 18.95 | 2.01 | 27.21 | 2.80 |
| | | | | | | Controls | | 15.02 | 1.10 | 24.12 | 2.30 |
| Elmoazen et al. (2021) ^[22] | 500 Hz Tone Burst (condensation) -Supra aural headphones | 5 | 95 dB nHL | 150 | 1- 1000 | PwMS with Brainstem lesions | Average across sides | 16.49 | 1.49 | 25.96 | 1.93 |
| | | | | | | PwMS without Brainstem lesions | | 15.21 | 1.57 | 23.97 | 2.06 |
| | | | | | | Controls | | 14.05 | 0.94 | 23.36 | 2.14 |
| Cochrane et al. (2021) ^[34] | Unspecified Tone Burst (?) – earphone unspecified | ? | ? | ? | ? | PwMS | ? | 13.70 | 1.30 | 21.10 | 2.60 |
| | | | | | | Controls | | 13.30 | 0.50 | 20.60 | 1.80 |

Abbreviations:

PR = Presentation Rate, PL = Presentation Level, Ave. = Number of Averages, BP = Band Pass, , \bar{x} = Mean, SD = Standard Deviation, dB SPL = Decibels Sound Pressure Level, dB HL = Decibels Heraing Level, dB nHL = Decibels normal Hearing Level, PwMS = Persons with Multiple Sclerosis, IA Diff. = Inter-aural Difference, ? = not reported. Cells Highlighted in Yellow indicate that "normalized amplitudes" were reported as opposed to absolute amplitudes reported by other studies. Cells Highlighted in Green indicate results were reported without specifying side or if they are averaged across sides.

Gür, Binkhamis, Kluk (2022)

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