



Étude de la symétrie de la réponse vestibulo-posturale chez des adolescentes ayant une scoliose idiopathique

Mémoire

Jean-Philippe Cyr

Maîtrise en kinésiologie - avec mémoire
Maître ès sciences (M. Sc.)

Québec, Canada

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Jean-Philippe Cyr

Sous la direction de :

Martin Simoneau, PhD

Résumé

La scoliose idiopathique de l'adolescence (SIA) est une déformation 3D de la colonne vertébrale, la plus fréquente en orthopédie pédiatrique. Elle peut créer de la douleur, une diminution de l'estime de soi et entraîner plusieurs complications comme des problèmes respiratoires et cardiaques. Si l'étiologie de la SIA est peu connue, il est admis qu'elle est multifactorielle et pourrait impliquer une asymétrie vestibulaire. L'objectif de ce mémoire était d'évaluer l'asymétrie de la voie vestibulospinale chez des adolescentes avec une SIA, par l'analyse spectrale entre l'activité vestibulaire évoquée et la réponse posturale.

Méthode: 7 adolescentes avec une SIA et 15 sans SIA ont reçu une stimulation vestibulaire électrique de type stochastique tout en se tenant debout sur une plateforme de forces. Différentes configurations des électrodes ont permis d'induire des stimulations binaurales ou monaurales (gauche et droite), ce qui a induit des changements dans les forces de réaction au sol. La cohérence vestibulo-posturale, la phase et la corrélation croisée entre l'activité vestibulaire et les forces de réaction au sol ont été calculées. Afin de soutirer davantage d'information sur la transformation sensorimotrice, nous avons calculé la norme et l'orientation du vecteur postural résultant. Finalement, nous avons exploré la relation entre l'asymétrie vestibulo-posturale et la sévérité de la scoliose.

Résultats: Les adolescentes avec une SIA ont montré une asymétrie dans la cohérence vestibulo-posturale, de même qu'une plus grande variabilité de la phase et un plus lent délai du pic de la corrélation croisée lors de la comparaison des conditions de stimulations monaurales droite et gauche. L'analyse du vecteur postural résultant a révélé une orientation déviée de l'espace intéraural lors des stimulations monaurales gauches. Toutefois, l'asymétrie observée semble être atténuée lors de stimulations binaurales.

Conclusion : Les résultats suggèrent une asymétrie de la transformation vestibulo-posturale chez les adolescentes avec une scoliose idiopathique.

Abstract

Adolescence idiopathic scoliosis (AIS) is a 3D deformation of the spine, the most common in pediatric orthopedics. It can cause pain, lower self-esteem, and lead to several complications such as pulmonary and cardiac problems. The etiology of AIS is little known, but it is believed to be multifactorial and could imply vestibular asymmetry. The objective of this dissertation was to assess the asymmetry of the vestibulospinal pathways in adolescent girls with AIS, using spectral analysis between the vestibular evoked activity and the postural response.

Methods: 7 adolescent girls with AIS and 15 healthy controls received a stochastic electrical vestibular stimulation (SVS) while standing on a force platform. Different electrodes configurations were used to induce binaural or monaural stimulation (left and right), which induced changes in ground reaction forces. Vestibulo-postural coherence, phase and cross-correlation between vestibular activity and ground reaction forces were calculated. To extract more information on sensorimotor transformation, we calculated the norm and the orientation of the resulting postural vector. Finally, we explored the relationship between vestibulo-postural asymmetry and the severity of scoliosis.

Results: Adolescent girls with AIS showed asymmetrical vestibulo-postural coherence, greater phase variability and a delayed peak of the cross-correlation when comparing the right and left monaural stimulation. During left monaural stimulation, the resulting postural vector also deviated from the interaural axis in the AIS group. The asymmetry observed, however, seems to be reduced during binaural stimulation.

Conclusion: The results suggest an asymmetry in the vestibulo-postural transformation in adolescent girls with idiopathic scoliosis.

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Liste des abréviations, sigles, acronymes

3D/3D: three dimensions/trois dimensions	ii
AIS/SIA : adolescence idiopathic scoliosis/scoliose idiopathique de l'adolescence.....	ii
CI/IC: confidence interval/intervalle de confiance	30
CoC: comparison of coherence/comparaison de cohérence.....	31
CTR/CTR: control/contrôle	30
EVS/SVE: electrical vestibular stimulation/stimulation vestibulaire électrique	16
GRF/FRS: ground reaction forces/forces de réaction au sol.....	22
RMS: root mean square/valeur moyenne quadratique	29
SVS: stochastic vestibular stimulation/stimulation vestibulaire stochastique	16
VEMP: vestibular evoked myogenic potentials/potentiel évoqué vestibulaire-musculaire ..	47

À mes grands-parents.

*« J'ai toujours aimé le désert. On s'assoit sur une dune de sable. On ne voit rien.
On n'entend rien. Et cependant quelque chose rayonne en silence... »*

– Antoine de Saint-Exupéry

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Avant-propos

Ce mémoire est présenté sous le format par insertion d'articles. Chacun des articles a été publié, soumis pour publication ou est en voie de l'être. Les références bibliographiques, la contribution relative de chacun des auteurs et l'état de soumission de chaque article sont rapportés ci-dessous. Le contenu des articles n'est pas différent des versions publiées ou soumises, mais la mise en page a pu être modifiée par souci d'harmonie. Les figures présentées dans ce mémoire ont toutes été créées ou adaptées à l'aide du logiciel libre de dessin vectoriel, Inkscape (<http://inkscape.org>), ou d'autres logiciels comme Matlab™ (<https://www.mathworks.com>), Microsoft® Office PowerPoint® (<https://products.office.com/powerpoint>) ou R (www.r-project.org).

Le présent mémoire comprend trois sections : le premier chapitre s'intitule « État des connaissances » et introduit la problématique de recherche ainsi que les concepts nécessaires à la compréhension du travail réalisé. Le deuxième chapitre s'intitule « Asymmetric vestibulo-postural response in adolescents with idiopathic scoliosis ». Il s'agit du cœur du mémoire, puisque c'est l'article principal qui découle de mes travaux de maîtrise. Je suis premier auteur de cet article. J'ai participé à la demande présentée au comité d'éthique, à la conceptualisation du projet, au recrutement des participants, à la collecte et aux analyses de données, de même qu'à la rédaction et à la révision de l'article. Les coauteurs de cet article sont Dr Pierre Mercier, Jean-Sébastien Blouin et Martin Simoneau. Le troisième chapitre s'intitule « Discussion générale ». Dans cette section, je discute plus largement des résultats découlant de mes travaux de maîtrise, de même que des perspectives pour de futurs projets.

En annexe se trouve également un autre article intitulé « Balance control mechanisms do not benefit from successive stimulation of different sensory systems », dont je suis aussi le premier auteur. L'article a été publié dans le journal *PLOS ONE* le 11 décembre 2019. L'article a été intégré au mémoire, car ces travaux ont été réalisés pendant ma maîtrise, et réfèrent à des concepts similaires et complémentaires à ceux présentés (comme le contrôle de l'équilibre et intégration

sensorimotrice). Lors de la réalisation de ce deuxième article scientifique, j'ai été impliqué dans la demande d'éthique, dans la conceptualisation, dans le recrutement des participants, dans la collecte et analyse de données, de même que dans la rédaction et la révision de l'article. Les coauteurs de cet article sont Noémie Ancil et Martin Simoneau.

Malheureusement, dû au contexte de la pandémie de la maladie à coronavirus (COVID-19), nous avons été forcés d'interrompre les collectes de données en cours, ce qui a empêché de compléter le groupe clinique. En conséquence, certains tests statistiques manquent de puissance, et ne nous permettent pas de répondre à certaines de nos hypothèses. Cependant, nous prévoyons reprendre les collectes de données et compléter le groupe clinique dès que le contexte de santé publique le permettra. Malgré tout, les résultats rapportés dans ce mémoire sont novateurs et permettent de mieux comprendre la réponse vestibulo-posturale chez des adolescentes atteintes d'une scoliose idiopathique.

Introduction générale

Les systèmes sensoriels sont présents et fonctionnent même avant la naissance. Toutefois, ils se développent et se raffinent pendant le développement, provoquant une réorganisation des réseaux neuraux sensorimoteurs et induisant des modifications cognitives permanentes (Alais et al., 2019). Par exemple, les voies ascendantes et descendantes qui assurent la communication entre les systèmes nerveux central et périphérique continuent leur développement bien après la naissance. L'interaction de l'humain avec son environnement dépend du fonctionnement de ces systèmes, et est assurée par les récepteurs sensoriels, les voies nerveuses et le système nerveux central. Cette interaction est essentielle à l'être humain afin qu'il puisse contrôler son équilibre, lui qui est fondamentalement instable (Winter, 1995). En effet la bipédie requiert un contrôle actif et continu de l'équilibre. Afin de stabiliser le corps, l'information provenant principalement des systèmes visuel, proprioceptif et vestibulaire est continuellement intégrée et pondérée en fonction de sa pertinence (Maurer et al., 2006; Oie et al., 2002; Peterka, 2002). Un déficit d'un de ces systèmes ou des mécanismes sensorimoteurs rend donc plus difficile le contrôle de l'équilibre.

En plus du contrôle de l'équilibre, la bipédie exige un contrôle postural adapté, et la colonne vertébrale a évolué en conséquence. La colonne vertébrale est une structure complexe du corps humain. Elle est constituée de la succession de trente-trois à trente-quatre vertèbres, de ligaments et de disques intervertébraux dans un arrangement qui permet le mouvement du rachis dans les trois plans. Elle permet de transmettre le poids de la tête, des membres supérieurs et du tronc aux membres inférieurs responsables du contrôle de l'équilibre. L'alternance de lordoses et de cyphoses dans le plan sagittal permet à la colonne vertébrale un meilleur amortissement des chocs et une plus grande flexibilité, tout en ne nuisant pas à ses propriétés de rigidité et de stabilité. L'importance de ces courbures varie d'un individu à l'autre (Liu, 2001; Platzer, 2014). Cependant, un mauvais alignement des vertèbres peut conduire à différentes déformations rachidiennes.

La déformation rachidienne la plus fréquente en orthopédie pédiatrique est la scoliose. Celle-ci est caractérisée par un déplacement latéral et une rotation des vertèbres créant une déformation en trois dimensions (Letellier et al., 2007). Chez des adolescentes atteintes de la scoliose idiopathique, plusieurs pistes semblent indiquer qu'une altération des mécanismes sensorimoteurs, dont le système vestibulaire, pourrait être impliquée dans l'étiologie.

Chapitre 1 : État des connaissances

1.1 La colonne vertébrale

Si on demandait à un architecte de disposer une colonne sur une base inclinée à 40° à l'horizontale, il vous proposerait de vous adresser ailleurs (...). Vous lui demandez de réaliser cet équilibre avec une pile de pièces articulées, de permettre et de contrôler des mouvements dans tous les plans de l'espace, le problème devient vertigineux (Stagnara, 1984).

La colonne vertébrale (Figure 1-1) est une structure complexe du corps humain. Elle est constituée de la succession de trente-trois à trente-quatre vertèbres, de ligaments et de disques intervertébraux, dans un arrangement qui permet le mouvement dans les trois plans de l'espace. Plus précisément, elle comprend cinq segments. Le premier, le segment cervical, comprend sept vertèbres qui forment une lordose. Le second segment, thoracique, comprend douze vertèbres qui forment une cyphose. Le troisième segment, lombaire, est constitué de cinq vertèbres qui forment une lordose, et repose sur les segments sacral (cinq vertèbres) et coccygien (quatre ou cinq vertèbres). Les vertèbres sacrales et coccygiennes sont fusionnées, et forment le sacrum et le coccyx. L'alternance de lordoses et de cyphoses dans le plan sagittal permet à la colonne vertébrale un meilleur amortissement des chocs et une plus grande flexibilité, tout en ne nuisant pas à ses propriétés de rigidité et de stabilité (Liu, 2001; Platzer, 2014).

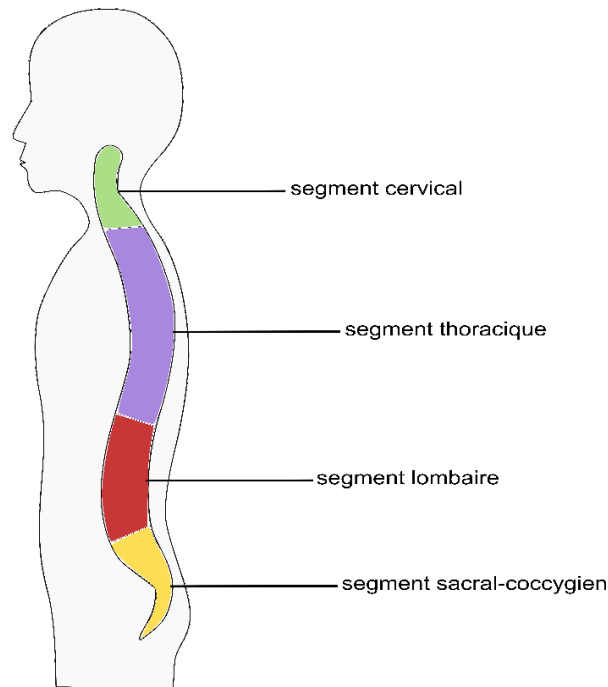


Figure 1-1: Simplification de la colonne vertébrale.

La colonne vertébrale permet de transmettre le poids de la tête, des membres supérieurs et du tronc aux membres inférieurs responsables du contrôle de l'équilibre. La charge est donc croissante en descendant le long du rachis, ce qui explique pourquoi la taille des vertèbres croît aussi. La tête et le tronc représentent à eux seuls près de 60% de la masse corporelle totale (Winter, 2009). Or, la masse d'un segment corporel et sa distance avec l'axe de rotation sont déterminantes de l'effort nécessaire pour déplacer ce segment (Borelli, 1680).

Comme le rachis est lui-même composé de plusieurs segments, sa stabilité peut être simplifiée en imaginant un *inukshuk* (empilement de pierres construit par les peuples inuit) ou une pile de blocs (Figure 1-2). Si les parties sont parfaitement alignées, la structure est en équilibre. Or, un mauvais alignement des segments conduit à des forces gravitaires inégalement distribuées. Si l'on pense à l'*inukshuk*, cela signifie l'effondrement, mais chez l'humain, ces forces sont compensées par les muscles et les ligaments. Ainsi, plus grand l'angle d'inclinaison d'un segment du

corps par rapport à la verticale, plus important l'effort musculaire nécessaire au maintien de l'équilibre (Broer, 1966).

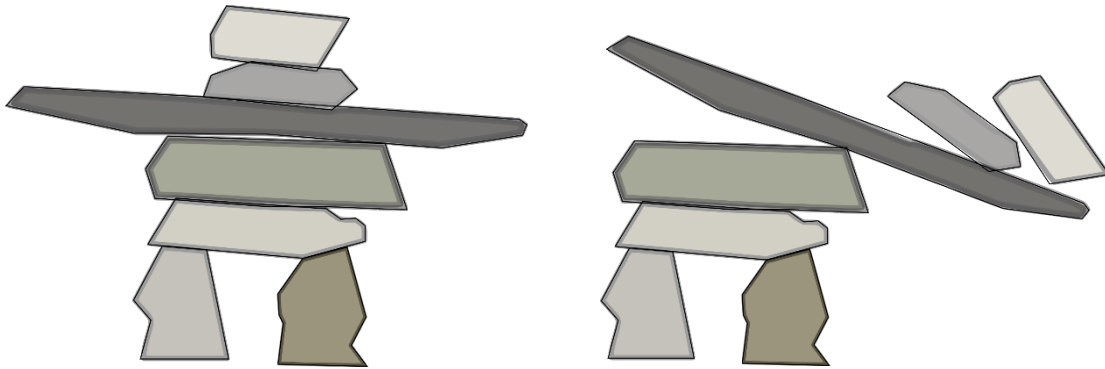


Figure 1-2: Inukshuk illustrant l'effet de l'alignement des segments sur l'équilibre.

Le rôle biomécanique de la colonne vertébrale est triple : assurer le mouvement des différentes parties du corps, transférer les charges, et protéger la moelle épinière et les racines nerveuses. Afin d'assurer ces rôles, la colonne vertébrale doit être stable. La stabilité du rachis est assurée par trois principaux sous-systèmes : les systèmes musculosquelettiques actif et passif, et le système neural et de rétroaction (Figure 1-3). Le système neural reçoit l'information des différents sens, détermine les actions nécessaires afin d'assurer la stabilité, et permet au système musculosquelettique actif d'établir la stabilité par l'ajustement de la tension musculaire. Cependant, un dysfonctionnement de l'un des trois sous-systèmes affecte la stabilité et peut induire une dégradation de la colonne vertébrale (Panjabi, 1992; Peter Reeves et al., 2007).

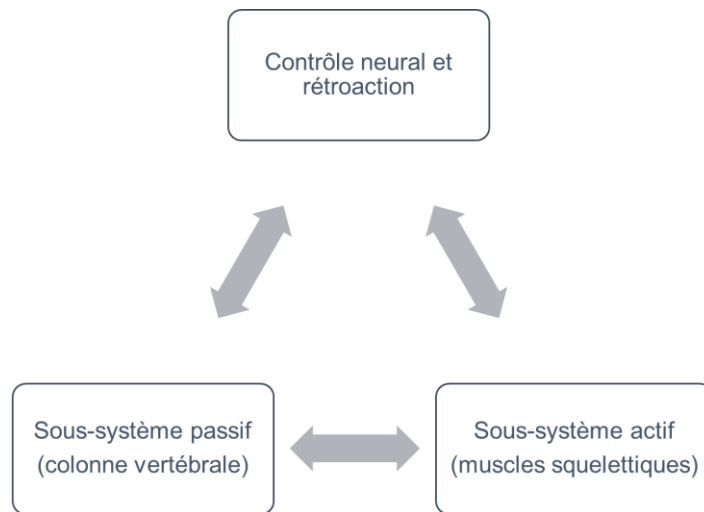


Figure 1-3: Les sous-systèmes assurant la stabilité de la colonne vertébrale (adapté de Panjabi, 1992).

1.2 La scoliose

La scoliose est une déformation rachidienne complexe, la plus fréquente en orthopédie pédiatrique. Elle se caractérise par une déviation latérale et une rotation des vertèbres, ce qui produit une déformation permanente, en trois dimensions, du rachis (Goldstein et al., 1973; Khouri et al., 2004; Letellier, et al., 2007; Robin, 1990; Wajchenberg et al., 2016). La déformation se compose d'une courbure primaire, que compensent souvent des courbures secondaires (Klineberg, 2017; Wajchenberg et al., 2016), ou « courbes compensatoires » (Goldstein, et al., 1973). L'angle de Cobb, une mesure du degré d'inclinaison des vertèbres dans le plan frontal, constitue la référence afin de quantifier la sévérité de la déformation, et ainsi prendre des décisions relatives aux traitements (Gstoettner et al., 2007; Morrissy, Goldsmith, Hall, Kehl, & Cowie, 1990). Dans la plupart des cas (80-88%), la scoliose est de nature idiopathique. Elle survient et progresse pendant la croissance, le plus souvent à la préadolescence et à l'adolescence (Goldstein, et al., 1973; Letellier, et al., 2007; Robin, 1990; Wajchenberg, et al., 2016). Les autres types de scolioses sont causés par des malformations congénitales, des maladies neuromusculaires, ou des pathologies osseuses ou de tissus conjonctifs (Letellier, et al., 2007). La scoliose

idiopathique est catégorisée selon le moment d'apparition, pouvant être infantile, juvénile, ou de l'adolescence (Wajchenberg, et al., 2016). La prévalence à la scoliose idiopathique de l'adolescence (SIA) varie de 0,4 à 3,9 % (Klineberg, 2017). La SIA touche plus souvent (près de dix fois) et plus sévèrement les filles que les garçons (Burwell, 2003; Letellier, et al., 2007).

Les déformations rachidiennes comme la scoliose entraînent souvent une distribution anormale des forces et une adaptation pathologique des tissus (Whiting et al., 2008). Non traitée, la scoliose risque de progresser et entraîner des douleurs chroniques au dos, l'apparition prématurée d'ostéoporose, des complications cardiorespiratoires, ou l'invalidité (Klineberg, 2017; Letellier, et al., 2007). Le traitement implique un suivi en orthopédie, et souvent le port d'un corset, mais aussi dans plusieurs cas une instrumentalisation de la colonne vertébrale qui nécessite une intervention chirurgicale coûteuse et possiblement morbide (Hawasli et al., 2015). Il importe donc de déterminer quels sont les mécanismes d'apparition et de développement de la SIA.

1.3 L'implication des mécanismes sensorimoteurs dans l'apparition et le développement de la scoliose

Si l'origine exacte de la SIA est inconnue, l'on sait qu'elle est multifactorielle, et peut comprendre des implications génétiques, endocriniennes, biomécaniques, neurologiques, ou métaboliques (Burwell, 2003; Goldstein, et al., 1973; Letellier, et al., 2007; Wilczynski et al., 2018). À ce jour, plusieurs pistes suggèrent que des dysfonctions sensorielles seraient liées à l'apparition et à l'évolution de cette déformation rachidienne. Parmi celles-ci, l'idée d'une implication vestibulaire accumule de plus en plus d'évidences (Hawasli, et al., 2015). Sans manipulation des informations sensorielles, les participants avec une SIA n'ont pas un contrôle de l'équilibre différent de participants sans SIA. Cependant, dans des situations où le contrôle sensorimoteur de l'équilibre devient plus exigeant (p. ex., lors de la manipulation de la qualité d'une entrée sensorielle), elles performant moins bien (Byl et al., 1993; Byl et al., 1997; Yamamoto et al., 1982). Pendant et après une

stimulation vestibulaire électrique, le contrôle de l'équilibre est altéré chez les adolescentes avec une SIA (Pialasse et al., 2015). Par ailleurs, pour maintenir l'équilibre lors de l'altération de la proprioception de la cheville, des adolescentes avec une SIA montrent des différences d'activation du cortex sensorimoteur. Une augmentation des fréquences thêta et une suppression des fréquences alpha, bêta et gamma semble indiquer une stratégie compensatoire de l'intégration sensorimotrice (Fortin et al., 2019). Des études en imagerie par résonance magnétique (IRM) montrent également des asymétries neuroanatomiques des aires corticales impliquées dans le contrôle sensorimoteur. Ces différences sont caractérisées par un plus grand volume des lobes pariétal, frontal et temporal chez des patients avec une scoliose (Liu et al., 2008), des régions pouvant être impliquées dans le contrôle sensorimoteur et la coordination (Fasold et al., 2002). Dès la fin des années 1970, Sahlstrand a observé une asymétrie vestibulaire chez les enfants atteints de scoliose idiopathique, et parlait déjà de ce phénomène comme d'un possible « mécanisme de déclenchement » de la courbure de la colonne vertébrale (Sahlstrand et al., 1979). Bien qu'intéressants, les résultats de cette étude sont toutefois limités par leur nature qualitative. De plus, la question demeure si l'asymétrie vestibulaire observée n'est pas une conséquence plutôt qu'une cause de la scoliose.

D'une part, l'argument le plus fort en faveur d'une implication vestibulaire dans l'apparition et le développement de la SIA vient d'études animales. Chez des têtards *Xenopus laevis*, une labyrinthectomie unilatérale peut induire une déformation permanente de la colonne vertébrale semblable à une scoliose sévère chez l'humain (Lambert et al., 2009; Lambert et al., 2013). Des résultats similaires ont été observés chez le rat *Wistar* (Barrios et al., 1992), ainsi que chez le hamster *syrien* et le poulet *Leghorn* (O'Kelly et al., 1999). L'hypothèse qu'une asymétrie persistante des voies descendantes pendant le développement pourrait altérer la croissance du squelette et provoquer des déformations scoliotiques a donc été émise. En effet, des différences latérales de l'encodage et de l'intégration des informations vestibulaires pourraient conduire à une asymétrie vestibulaire fonctionnelle (Simoneau et al., 2009; Woo et al., 2019). Un déséquilibre vestibulaire induit, via les voies

vestibulospinales et réticulospinales, une réponse réflexe et un tonus asymétrique des muscles squelettiques (Lambert, et al., 2009). De ce tonus asymétrique pourrait résulter une déviation et une torsion du tronc vers le côté où le tonus est plus faible (Sahlstrand, et al., 1979). Bien sûr, il est difficile d'extrapoler directement ces résultats chez l'animal à l'être humain. Mais ensemble, ces études renforcent l'idée d'un lien de cause à effet entre une dysfonction vestibulaire et l'apparition de la SIA.

D'autre part, si la scoliose provoquait une asymétrie vestibulaire, et non l'inverse, il faudrait qu'il existe un mécanisme neural grâce auquel le système vestibulaire pourrait recevoir des informations provenant de la colonne vertébrale. Cependant, un tel mécanisme de rétroaction ascendante entre la colonne vertébrale et les organes vestibulaires n'est pas clairement défini (Hawasli, et al., 2015). De plus, des études s'intéressant aux patients avec lésion complète de la moelle épinière ou atteints de paraplégie n'ont pas observé de différences dans la perception de la verticalité (Barra et al., 2010; Joassin et al., 2010). Dans le cas où une dysfonction vestibulaire serait une conséquence de la scoliose, il serait attendu de retrouver cette caractéristique dans d'autres conditions où la voie vestibulospinale est atteinte. Aussi, les dysfonctions sensorimotrices semblent propres à la scoliose idiopathique de l'adolescence. En effet, les patientes atteintes de la scoliose congénitale ne présentent pas de problème d'équilibre ou vestibulaire (Herman et al., 1985).

1.4 L'intégration multisensorielle et le contrôle de l'équilibre

Même en l'absence de déformation rachidienne, l'être humain est fondamentalement instable. Afin de réduire les oscillations posturales, et ainsi se rapprocher d'un état d'équilibre, les informations provenant des systèmes proprioceptif, visuel, vestibulaire, ainsi que des mécanorécepteurs de la voute plantaire sont continuellement combinées (Bronstein, 1986; Bronstein et al., 1986; Kavounoudias et al., 1999; Magnusson et al., 1990). Le contrôle de l'équilibre, quoiqu'ayant l'air trivial au premier abord, est en réalité complexe et dépend de l'intégration multisensorielle. En général, il est admis qu'il repose principalement sur

les informations proprioceptives (Diener et al., 1984; Horak et al., 2002). En effet, leur contribution est estimée à plus de 60 % (Lord et al., 1991; Peterka et al., 1995; Simoneau et al., 1995; van Deursen et al., 1999). Mais bien que les systèmes sensoriels aient longtemps été perçus comme distincts, l'on admet de plus en plus l'existence d'interactions entre les sens. Par exemple, des projections vestibulaires ont été identifiées dans les cortex somatosensoriels primaire et secondaire (Bottini et al., 1994; Fasold, et al., 2002) ainsi que dans les cortex moteur primaire et prémoteur (Bense et al., 2001; Emri et al., 2003; Fasold, et al., 2002). Au-delà des jonctions anatomiques, il pourrait y exister une interaction fonctionnelle entre ces sens. Cette idée est supportée par les résultats de Day et Cole (2002), qui ont montré qu'une stimulation vestibulaire électrique induit une réponse posturale de plus grande amplitude chez un patient atteint de pertes somatosensorielles sévères comparativement à des participants en santé. Les résultats de leur étude suggèrent que le gain des entrées sensorielles serait modulé de façon dynamique en fonction de leur pertinence et de la disponibilité des autres informations sensorielles (Day et al., 2002). Des études psychophysiques ont aussi révélé que la détection des stimuli cutanés peut être facilitée par une stimulation vestibulaire (Ferre et al., 2011). D'autres auteurs ont montré une augmentation de la dépendance visuelle chez des personnes atteintes de névrite vestibulaire (Cousins et al., 2014). Ainsi, de plus en plus d'évidences suggèrent que les traitements des informations visuelles, somatosensorielles et vestibulaires s'influencent mutuellement. Un peu à la manière d'un scrutin proportionnel, chaque vote (système sensoriel) aurait un poids. Cependant, le résultat final dépendrait de l'ensemble des votes (Day, et al., 2002). Le poids de chaque système sensoriel est modulé, lui, selon un modèle Bayésien. Autrement dit, le système nerveux central accorde un poids plus important à l'entrée sensorielle dont la variabilité est la plus faible, selon un modèle de rétroaction simple (Peterka, 2002).

1.5 Le système vestibulaire et le contrôle de l'équilibre

Le système vestibulaire est phylogénétiquement parlant le plus ancien système sensoriel (Haines et al., 2018; Sadeghi et al., 2015). Pourtant, possiblement parce que l'appareil vestibulaire n'est pas visible, il fut le dernier sens à être découvert (Cohen, 1999). Dès la première moitié du 19^e siècle, Flourens, Purkinje, Menière ainsi que Goltz ont établi des liens entre les canaux semi-circulaires de l'oreille interne et le contrôle de l'équilibre. Plus tard, vers 1870, Josef Breuer, Ernst Mach et Alexander Crum ont avancé que le liquide contenu dans ces canaux était impliqué dans la perception de l'automouvement (Lopez et al., 2014). Aujourd'hui, il est bien établi que le contrôle de l'équilibre dépend en partie du système vestibulaire. Le système vestibulaire détecte continuellement les accélérations linéaires et angulaires de la tête dans les trois plans de l'espace grâce aux organes otolithiques et aux canaux semi-circulaires, respectivement (Cathers et al., 2005; Fitzpatrick et al., 2004; Sadeghi, et al., 2015). Il est composé de cinq structures principales (Figure 1-4) que sont les trois canaux semi-circulaires de l'oreille interne (horizontal, antérieur et postérieur), sensibles aux mouvements rotatifs, et les deux organes otolithiques (utricule et saccule), sensibles aux mouvements translatifs.

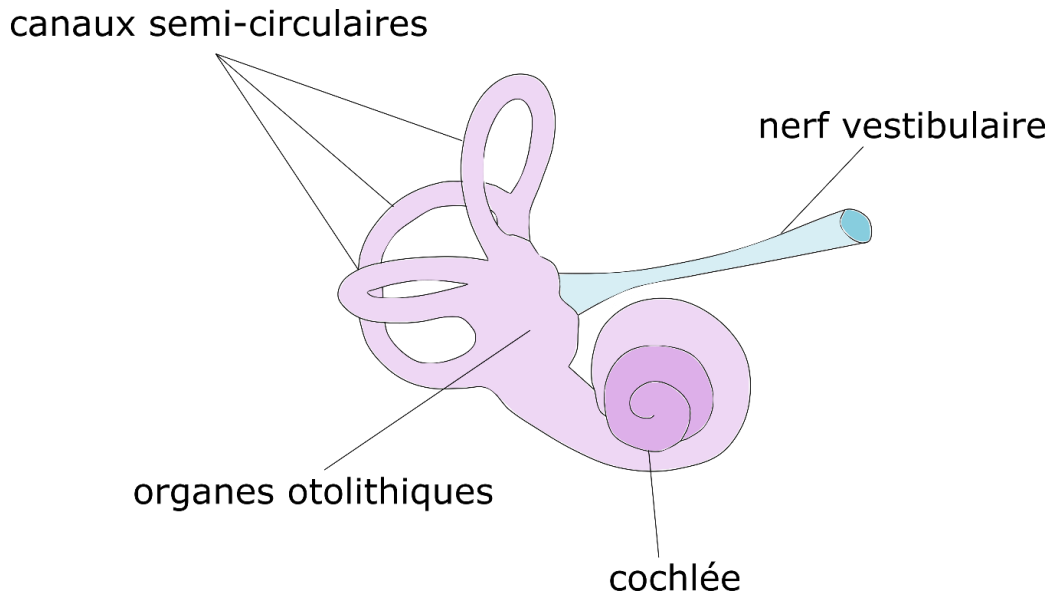


Figure 1-4: Les composantes du système vestibulaire.

Les signaux vestibulaires naissent dans les labyrinthes de l'oreille interne, où se trouvent les récepteurs sensoriels vestibulaires et auditifs. Les récepteurs sensoriels vestibulaires sont activés par le caractère inertiel et viscoélastique d'un fluide, l'endolymphe, qui remplit cette structure (Cohen, 1999; Héroux et al., 2015; Sadeghi, et al., 2015). Les cils présents dans les utricules permettent de transformer les stimuli mécaniques en influx nerveux (Hudspeth et al., 2013). Les influx bilatéraux sont combinés de sorte qu'un neurone recevant une excitation d'un canal semi-circulaire reçoit également une inhibition du canal controlatéral complémentaire (Baker et al., 1984). L'asymétrie de ces influx est comparée par le système nerveux central, qui détermine alors les accélérations linéaire et angulaire de la tête (Hawasli, et al., 2015). Chez l'humain et chez l'animal, des études ont montré que les mouvements habituels de la tête, et par conséquent les stimuli vestibulaires, étaient de basses fréquences, allant de 0 à 20 Hz, et pouvaient atteindre environ 30 Hz lors d'activités sportives (Carriot et al., 2014; Grossman et al., 1988).

Il existe des neurones vestibulaires de premier et de second ordre. Les neurones vestibulaires de premier ordre sont la source majeure des afférences vestibulaires.

Ils sont connectés aux canaux semi-circulaires et aux organes otolithiques, et projettent dans les noyaux vestibulaires. Les neurones vestibulaires de second ordre n'atteignent pas directement les structures cérébrales, mais passent d'abord par le thalamus (Lopez et al., 2005). Les influx vestibulaires sont à l'origine d'ajustements posturaux et de la stabilisation de la tête et de la vision. Ils permettent un meilleur contrôle de l'équilibre (McGeehan et al., 2017) en ayant une influence sur les muscles squelettiques (Dickman, 2018). Les influx vestibulaires rejoignent la moelle épinière, les noyaux oculomoteurs, et les aires corticales vestibulaires via les voies ascendantes et descendantes vestibulospinale, vestibulooculaire et vestibulocorticale (Lopez et al., 2011).

1.6 Les voies vestibulospinales

La moelle épinière est la voie de communication entre les systèmes nerveux central et périphérique. Elle s'étend du foramen magnum à la première ou deuxième vertèbre lombaire. Son centre, la matière grise, est composé de corps cellulaire des neurones et est entouré de fibres neurales qui constituent la matière blanche. La matière blanche de la moelle épinière comprend trois grandes régions, les funiculus postérieur, antérieur et latéral. Chacune de ces régions comprend des voies et des fascicules. La moelle épinière conduit donc l'information sensorielle des membres inférieurs et supérieurs, du tronc et de la plupart des viscères via les voies ascendantes et descendantes. Ces voies sont souvent nommées selon leur origine et leur terminaison. Les funiculus antérieur et latéral comprennent les fibres vestibulospinales médiale et latérale, respectivement, qui sont liées aux noyaux vestibulaires médial et latéral, et forment les voies vestibulospinales (Figure 1-5) (Haines et al., 2018). Les neurones de la voie vestibulospinale médiale innervent principalement les muscles du cou. La voie vestibulospinale latérale, elle, projette à tous les niveaux de la moelle épinière (tous les segments de la colonne vertébrale), de façon ipsilatérale et controlatérale, et coordonne ainsi différents groupes musculaires assurant la stabilisation du centre de masse et le contrôle postural (Dickman, 2018).

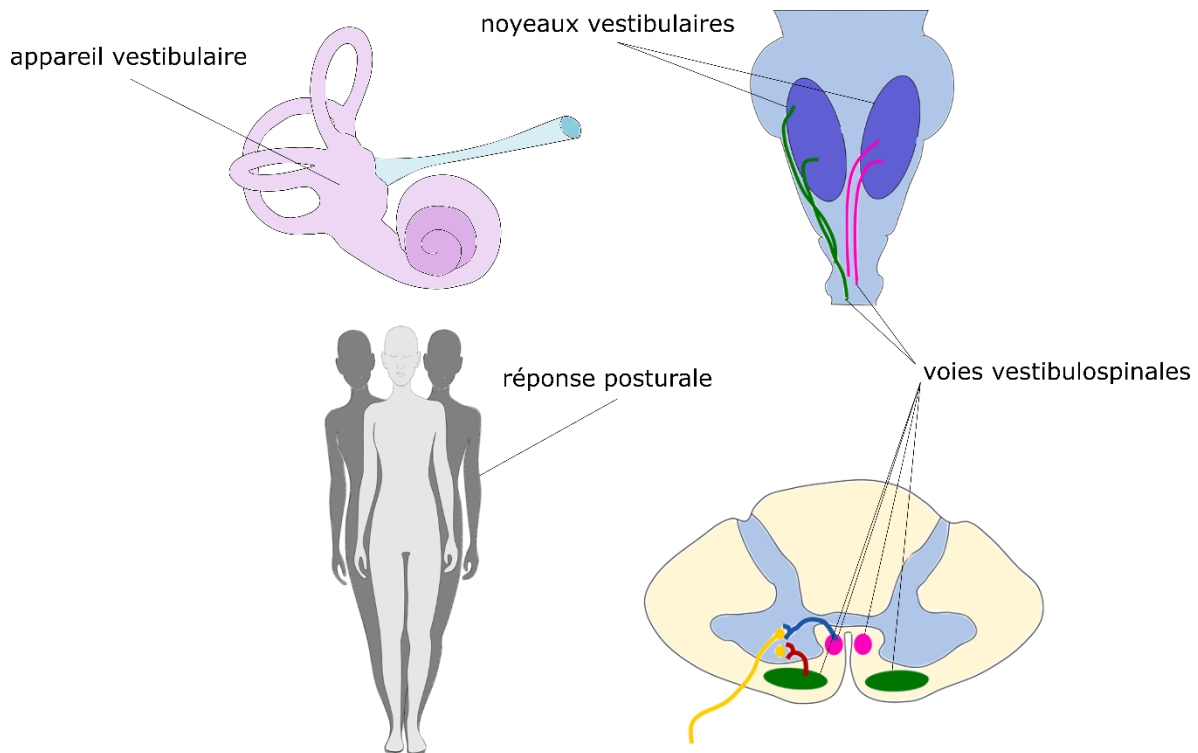


Figure 1-5: Les voies vestibulospinales assurant la communication des influx vestibulaires aux muscles posturaux.

1.7 La stimulation vestibulaire électrique

Au début des années 1900, influencé par les travaux du siècle précédent, l'otologiste austro-hongrois (Prix Nobel de Médecine et prisonnier de guerre par la Russie) Robert Bárány a développé la stimulation vestibulaire calorique. En effet, Bárány a été le premier à comprendre que l'injection d'eau chaude et d'eau froide dans les conduits auditifs des patients provoquait un phénomène de convection du fluide endolymphatique des canaux semi-circulaires, qui à son tour activait les cils de l'appareil vestibulaire (Lopez, et al., 2014). Un problème avec la stimulation vestibulaire calorique, pour des protocoles de recherche, est que l'effet n'est maximal que 80 s après l'injection d'eau, et peut durer jusqu'à 15 minutes (Proctor, 1985). Or, une autre façon d'altérer les informations vestibulaires, et ainsi d'étudier le fonctionnement des voies vestibulospinales, consiste à moduler artificiellement la fréquence de décharge du nerf vestibulaire, en appliquant un courant électrique transcutané aux processus mastoïdiens à l'aide d'électrodes bipolaires binaurales

(Fitzpatrick, et al., 2004; Goldberg et al., 1982; Héroux, et al., 2015; McGeehan, et al., 2017). Une telle stimulation provoque une augmentation de la fréquence de décharge du nerf vestibulaire du côté de la cathode, et une diminution de celle-ci à l'anode (Fitzpatrick, et al., 2004; Goldberg et al., 1984).

1.8 La réponse posturale à une stimulation vestibulaire électrique

Lorsque soumise à une stimulation vestibulaire électrique, une personne a une illusion de déstabilisation de la tête vers la cathode, un réflex musculaire distinct et une réponse posturale en direction de l'anode (Fitzpatrick et al., 2004; Goldberg, et al., 1984; Héroux, et al., 2015). La réponse posturale est complexe et dépend de la tâche, de la posture et de la disponibilité d'autres informations sensorielles (Wardman et al., 2003). D'après le modèle de sommation vectorielle des afférences vestibulaires proposé par Fitzpatrick et Day (Figure 1-6), une stimulation vestibulaire bipolaire binaurale provoque une illusion de rotation autour d'un vecteur sagittal pointant vers l'arrière et orienté à $\sim 19^\circ$ au-dessus du plan de Reid (Fitzpatrick, et al., 2004; Mian et al., 2009). La rotation se produit habituellement dans la direction intéaurale, perpendiculaire à l'orientation de la tête (Lund et al., 1983; Nashner et al., 1974).

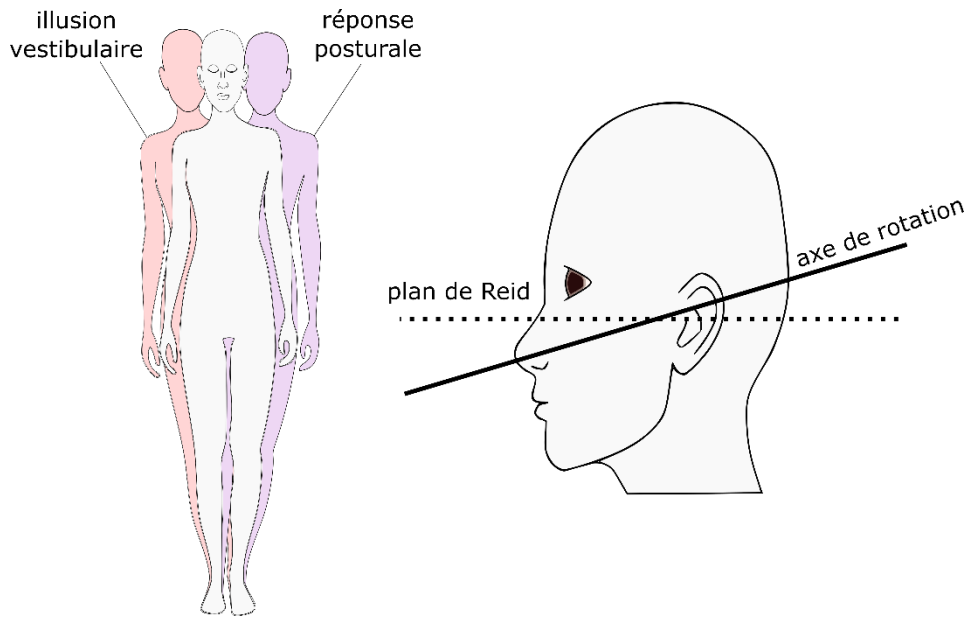


Figure 1-6: Illusion vestibulaire et réponse posturale induites par une stimulation bipolaire binaurale (adapté de Fitzpatrick et al., 2004).

Au cours des dernières décennies, la stimulation vestibulaire électrique (SVE) a été utilisée afin d'étudier le contrôle sensorimoteur de l'équilibre (Day, 1999). Dakin et collaborateurs ont aussi montré qu'une stimulation vestibulaire de type stochastique (SVS) est pertinente pour ce genre d'études. En plus de prévenir le biais d'anticipation, le signal à fréquences multiples de la SVS permet l'analyse fréquentielle et l'obtention de la fonction de transfert entre la stimulation vestibulaire et la réponse posturale. Elle offre en plus un meilleur ratio signal/bruit (Dakin et al., 2007; Mackenzie et al., 2018). La réponse posturale globale peut être analysée à l'aide des forces de réaction au sol, qui reflètent les mécanismes de transformation sensorimotrice (Mian, et al., 2009).

1.9 La cohérence

Dans les dernières décennies, des auteurs ont mesuré une asymétrie musculaire chez des patients atteints d'une SIA (Cheung et al., 2005; de Oliveira et al., 2011;

Farahpour et al., 2015). Un problème avec la mesure de l'asymétrie musculaire est qu'elle pourrait résulter de la déformation structurale de la colonne vertébrale. De surcroît, celle-ci ne renseigne pas sur la communication entre l'activité du cerveau, la moelle épinière et les muscles. Or, les signaux dans une série temporelle peuvent être présentés dans le domaine temporel ou fréquentiel. Le premier représente l'évolution d'un signal en fonction du temps, alors que le second, le nombre de cycles en une seconde, en Hertz (Hz) (Cohen, 2017). La mesure de la cohérence vestibulo-posturale permet de calculer le niveau de corrélation, dans le domaine fréquentiel, entre l'activité évoquée de l'appareil vestibulaire, la moelle épinière et les forces de réaction au sol traduisant une réponse posturale globale (ensemble de contractions musculaires réflexes ou volontaire). Elle permet ainsi d'évaluer le fonctionnement des voies descendantes, sans être influencée par l'amplitude respective des signaux. La cohérence représente une mesure de la relation linéaire, dans le domaine fréquentiel, entre deux signaux continus (Cohen, 2017; Conway et al., 1995; Halliday et al., 1995; Kramer et al., 2016).

La mesure de la cohérence repose grandement sur les principes proposés par Joseph Fourier. Le théorème de Fourier stipule que tout signal peut être décomposé en plusieurs sinus de fréquences, d'amplitudes et de phases distinctes. La transformée de Fourier consiste alors à déterminer les coefficients de Fourier en calculant le produit scalaire entre plusieurs sinus complexes (de nombre égal au nombre d'échantillons) et le signal, et décrit ainsi le spectre fréquentiel (Cohen, 2017; Fourier, 1822). Similaire au coefficient de corrélation, la mesure de la cohérence (Équation 1-1) varie de zéro à un, zéro témoignant de l'absence de relation linéaire entre les fréquences des deux signaux, et signifiant que les variables sont indépendantes l'une de l'autre (Cohen, 2017; McGeehan, et al., 2017; Rosenberg et al., 1989). La relation entre les signaux dépend strictement de la puissance à une fréquence donnée, ce qui constitue le plus grand avantage de l'analyse de cohérence, puisqu'elle est ainsi insensible à l'amplitude des signaux étudiés (Glaser et al., 1976). Pour ces raisons, la mesure de la cohérence est de plus en plus utilisée afin d'étudier la synchronisation entre le cortex sensorimoteur et le contrôle du mouvement (Halliday, et al., 1995; Rosenberg, et al., 1989).

$$C_{xy} = \frac{|G_{xy}(f)|^2}{G_{xx}(f) G_{yy}(f)}$$

Equation 1-1: Calcul de la cohérence

Dans l'équation de la cohérence ci-dessus, $G_{xy}(f)$ représente la densité spectrale commune aux signaux x et y, alors que $G_{xx}(f)$ et $G_{yy}(f)$, la densité spectrale propre à chacun des signaux x et y.

1.10 La quantification de la norme et l'orientation de la réponse posturale

La mesure de la cohérence vestibulo-posturale représente assurément un intérêt pour l'étude des mécanismes sensorimoteurs chez des adolescentes atteintes de la SIA. Or, dans le cadre de ce mémoire, la cohérence est calculée à partir de l'activité vestibulaire évoquée et des forces de réaction au sol. Les forces de réaction au sol sont mesurées à l'aide d'une plateforme de forces, capable de mesurer les forces selon trois axes (antéropostérieur, médiolatéral et vertical). La cohérence vestibulo-posturale, dans ce cas, n'informe que par rapport à deux référentiels : les axes médiolatéral et antéropostérieur des forces de réaction au sol. En utilisant la fonction de densité cumulée obtenue par l'analyse fréquentielle d'Halliday et collaborateurs, Mian et Day (2009) ont combiné une multitude de référentiels entre les axes médiolatéral et antéropostérieur, et déterminé la norme et l'orientation de la réponse posturale lors d'une SVS. La densité cumulée représente une mesure de la corrélation croisée. Pour les signaux non corrélés, la densité cumulée a une valeur nulle (Mian, et al., 2009). Ainsi, en partant de l'axe médio-latéral, les auteurs ont créé un axe de rotation, $ROT(\theta)$, allant de 0° à 360° . Pour chaque degré de rotation, la force résultante (Équation 1-2) était obtenue selon :

$$F_{ROT(\theta)}(s) = F_X(s) * \cos \theta + F_Y(s) * \cos \theta$$

Equation 1-2 : Calcul de la force résultante (FROT(Θ)) selon l'évolution de l'axe de rotation ROT(Θ).

Selon l'équation ci-dessus, $F_X(s)$ et $F_Y(s)$ représentent les séries temporelles des forces de réaction au sol dans les axes médiolatéral et antéropostérieur, respectivement, et θ représente l'incrément de rotation.

Dans la méthode décrite par Mian et Day, l'angle pour lequel la latence moyenne de la force résultante était maximale était considéré comme étant l'orientation de la réponse posturale (Mian, et al., 2009).

1.11 Objectifs et hypothèses

L'objectif de ce mémoire de maîtrise consiste à étudier le fonctionnement et l'asymétrie des voies vestibulospinales chez des adolescentes avec une scoliose idiopathique, en étudiant la réponse vestibulo-posturale lors de stimulations vestibulaires stochastiques bipolaires monaurales (unilatérales) et binaurales (bilatérales). Nous émettons l'hypothèse qu'un couplage asymétrique (c.-à-d., différence de cohérence entre une stimulation vestibulaire monaurale droite et gauche) entre l'activité vestibulaire évoquée et la réponse posturale indiquera une altération vestibulo-posturale chez des adolescentes ayant une scoliose idiopathique. De plus, nous émettons l'hypothèse que l'orientation de la réponse posturale (c.-à-d., direction du vecteur résultant) des adolescentes avec une scoliose idiopathique sera déviée par rapport à l'axe intéaural et que la norme (c.-à-d., amplitude du vecteur résultant) sera asymétrique, lors de stimulations vestibulaires monaurales droites et gauches.

Chapitre 2 : Asymmetric vestibulo-postural response in adolescents with idiopathic scoliosis

Jean-Philippe Cyr^{1,2},

Pierre Mercier³, MD,

Jean-Sébastien Blouin⁴, PhD,

Martin Simoneau^{1,2}, PhD,

¹ Faculté de Médecine, Département de Kinésiologie, Université Laval, Québec, Canada

² Centre interdisciplinaire de recherche en réadaptation et intégration sociale (Cirris) du CIUSSS de la Capitale Nationale, Québec, Canada

³ Clinique d'orthopédie pédiatrique de Québec, Québec, Canada

⁴ School of Kinesiology, University of British Columbia, Vancouver, British Columbia, Canada

2.1 Résumé

La scoliose idiopathique de l'adolescence (SIA), une déformation du rachis, pourrait comprendre une altération du traitement vestibulaire. Pour évaluer le fonctionnement des voies vestibulospinales, nous avons étudié la réponse posturale induite par l'activité vestibulaire évoquée. **Méthode:** Les participantes (7 avec une SIA et 15 sans SIA) ont reçu une stimulation vestibulaire stochastique (SVS) en se tenant debout sur une plateforme de forces. Une SVS bipolaire binaurale ou monaurale a induit des changements dans les forces de réaction au sol. La cohérence vestibulo-posturale, la phase et la corrélation croisée entre la SVS et les forces ont été calculées, en plus de la norme et l'orientation du vecteur postural résultant. **Résultats:** Les résultats montrent une asymétrie vestibulo-posturale chez les adolescentes avec une SIA, et une réponse posturale déviée par rapport à l'espace intéraural. **Conclusion:** Dans l'ensemble, les résultats suggèrent une

asymétrie dans la transformation vestibulo-posturale chez les adolescentes avec une SIA.

2.2 Abstract

Adolescent idiopathic scoliosis (AIS), a deformation of the spine, could include alterations in vestibular processing. To assess the functioning of the vestibulospinal pathways, we studied the postural response induced by the evoked vestibular activity. **Methods:** Participants (7 with AIS and 15 without AIS) received vestibular stochastic stimulation (SVS) while standing on a force platform. Bipolar binaural or monaural SVS induced changes in ground reaction forces (GRF). Vestibulo-postural coherence, phase and cross-correlation between SVS and forces were calculated, in addition to the norm and orientation of the resulting postural vector. **Results:** The results show a vestibulo-postural asymmetry in adolescent girls with AIS, and a postural response deviated from the intestinal space. **Conclusion:** Overall, the present results suggest an asymmetrical vestibulo-postural transformation in adolescent girls with idiopathic scoliosis.

2.3 Introduction

Adolescent Idiopathic scoliosis (AIS) is a complex spinal deformity, the most common in pediatric orthopedics. It is characterized by a lateral deviation of the spine and a rotation of the vertebrae (Burwell, 2003; Goldstein, et al., 1973; Letellier, et al., 2007; Robin, 1990; Wajchenberg, et al., 2016). The exact origin of AIS is unknown, but it is suspected to be multifactorial, and may include genetic, endocrine, biomechanical, neurological, or metabolic alterations (Goldstein, et al., 1973; Lowe et al., 2000; Wilczynski, et al., 2018). Over the past 40 years, authors have investigated the implication of neurological mechanisms in its etiology (Lowe, et al., 2000), and suggested that AIS could involve a dysfunction of the sensorimotor mechanisms (Byl, et al., 1993; Keessen et al., 1992; Lowe, et al., 2000; O'Beirne et

al., 1989), including the vestibular system (Sahlstrand, et al., 1979; Sahlstrand et al., 1979).

During quiet upright standing, when sensorimotor control becomes more challenging, participants with AIS show poorer balance control compared to healthy controls (Byl, et al., 1993). Altered balance control has also been reported during and after alteration in vestibular information or ankle proprioception in adolescents with AIS (Pialasse, et al., 2015; Simoneau et al., 2006; Simoneau et al., 2006). Moreover, asymmetries in the cortical areas (i.e., parietal and frontal lobes), related to sensorimotor control and coordination, are characterized by a greater volume in participants with AIS (Liu, et al., 2008). These observations suggest that sensorimotor control alteration could be a potential cause of AIS.

The suggestion of an association between sensorimotor control impairment, vestibular asymmetry and spine deformation has been demonstrated using animal models. For instance, vestibular or brainstem lesions induced deformation of the spine in *Xenopus* frogs, *Wistar* rats, *Syrian hamsters* and *White leghorn chickens* (Barrios, et al., 1992; Lambert, et al., 2013; O'Kelly, et al., 1999). These observations suggest that an alteration in the functioning of the descending pathways can cause spine deformation. Indeed, vestibular asymmetry, induced following unilateral labyrinthectomy in *Xenopus* frogs, translated into an asymmetrical neural drive to axial musculature, causing spine deformation with similar characteristics to AIS. Moreover, the side of the scoliotic curve matched the side of the vestibular lesion (Lambert, et al., 2009, Lambert, et al., 2013). Other studies have reported morphological asymmetries in the semicircular canals in patients with AIS (Hitier et al., 2015; Shi et al., 2011). The asymmetries in the semicircular canals, however, do not necessarily translate into an asymmetrical functioning of the vestibulospinal pathways. Therefore, it is of interest to investigate further if vestibulospinal asymmetry could be a potential cause of AIS.

A non-invasive way to study the functioning of the vestibulospinal pathways is to modulate the firing rates of the vestibular nerves. Applying an electrical current through the mastoid processes activates the primary vestibular afferents from all

semicircular canals and the otoliths via activation of the hair cells or afferents (Goldberg, et al., 1984). Bipolar binaural electrical vestibular stimulation causes an increase in the firing rate of the vestibular nerve on the cathode side, and a decrease on the anode side (Goldberg, et al., 1982). This differential firing rate creates an illusion, that is a net virtual rotation around a vector pointing posteriorly with an angle of $\sim 19^\circ$ above Reid's plane (Fitzpatrick, et al., 2004; Goldberg, et al., 1982). This creates an illusion of head roll in head-centered coordinates, leading to a postural response in the opposite direction. This postural response is complex, and it depends on the task, posture, and availability of other sensory information (Day, et al., 2002; Day et al., 1997; Fitzpatrick et al., 1996; Marsden et al., 2003; Wardman, et al., 2003). By placing one electrode on one mastoid process and the other on the seventh cervical vertebrae's spinous process, it is also possible to evaluate the functioning of the right and left vestibular pathways independently (Day et al., 2010). Using monaural electrical vestibular stimulation, authors have compared the direction recognition threshold of AIS patients to healthy adolescents (Woo, et al., 2019). Patients with AIS showed higher and asymmetrical vestibular detection threshold in comparison to controls. This result supports the suggestion that alteration in processing vestibular afferents to perceive head motion may be a potential cause of AIS (Simoneau, et al., 2009; Woo, et al., 2019).

The communication between the vestibular nuclei, the spinal cord and the muscles can be studied by measuring the coherence and the cross-correlation between the vestibular evoked activity and the induced postural response (Dakin, et al., 2007). Similar to the correlation coefficient, the coherence between two signals varies from zero to one, zero indicating the absence of a linear relationship between the frequencies of the two signals, meaning that the variables are independent of one another (Cohen, 2017; Rosenberg, et al., 1989). The relationship between the signals depends on the power at a given frequency. The analysis of coherence is increasingly used to study the interaction between physiological signals and sensorimotor control (Halliday, et al., 1995; Rosenberg, et al., 1989). Compared to pulse-step electrical stimulation, stochastic vestibular stimulation (SVS) allows to estimate, through spectral analysis, the transfer function between SVS and evoked

postural response (Dakin, et al., 2007). In the current study, we calculated the coherence between vestibular evoked signals and postural responses to characterize the functioning of the right and left vestibulospinal pathways of AIS patients and controls. To quantify the direction and amplitude of the vestibular-evoked postural response, we calculated the cross-correlation between the SVS and postural response signals (Mian, et al., 2009). The norm and orientation of the vestibular-evoked postural response vector provides information about the vestibulo-postural transformation in patients with AIS and controls (Dalton et al., 2017; Mackenzie, et al., 2018).

The aim of this study was to assess if the functioning of the right and left vestibular pathways were asymmetrical in AIS patients. Furthermore, we investigated the quality of the vestibulo-postural transformation. If vestibulo-postural impairment is a potential cause of AIS, asymmetrical coupling between vestibular evoked activity and postural response will be observed in AIS compared to controls. Further, it is expected that asymmetrical neural drive to torso muscles will likely alter the vestibulo-postural transformation. Consequently, we also hypothesized that the orientation of the vestibular-evoked postural response of AIS patients will be deviated with respect to right-left interaural axis and the norm will be asymmetrical.

2.4 Methods

2.4.1 Participants

In total, twenty-two adolescents were involved in this study. A striking feature of AIS is that severe scoliosis (Cobb angle $> 40^\circ$) is 7.2 times more common in girls compared to boys, and girls are also 8 times more likely to progress to a curve that requires treatment (Konieczny et al., 2013; Miller et al., 2001). These sex-differences led us to recruit only girls to attenuate a possible effect of genetics on the results. Participants were enrolled into two groups. The AIS group was composed of seven adolescents with a diagnosis of AIS. Except for the spinal deformity, these adolescents were healthy. They were recruited through a pediatric orthopedics medical clinic, and the diagnosis and assessment of the severity of the spine deformation (i.e., Cobb angle by means of X-rays) were ensured by pediatric orthopedic surgeons. Patients with AIS were enrolled only if their spine deformity had a Cobb angle $\geq 25^\circ$. Access to medical information was provided with written permission of the legal guardians. The control group was composed of 15 healthy adolescents. All participants had no known history of neurological or musculoskeletal disorders (except for the spine deformity in the AIS group).

The statistical analysis (unpaired t-test) of the anthropometric characteristics of the participants (Table 2-1) revealed no difference between groups for age, weight, height, pain status, or frequency of physical activities (unpaired t-test: $p > 0.05$). Participants from both groups reported practicing similar activities, such as ice hockey, ski, dance, basketball, and volleyball. For five AIS patients, the main curve was right thoracic, while for the other two it was left thoraco-lumbar. Six patients out of seven had compensatory lower curves.

Table 2-1: Group anthropometric characteristics, pain status and the frequency of physical activity.

	AIS	CTR	P value
	Mean [SD]	Mean [SD]	
Age (years)	14 [1.9]	13 [1.5]	0.29
Height (cm)	161.8 [5.0]	157.9 [9.5]	0.27
Weight (kg)	54.9 [8.8]	51.1 [11.6]	0.52
Pain	0.9 [0.4]	0.4 [0.8]	0.52
Physical activities (h/w)	3.6 [1.9]	3.0 [1.3]	0.44
Cobb angle Thoracic/Thoracolumbar or lumbar (°)	29.2 [8.6] /		
	26.8 [11.7]	--	--

Prior to the experiment, participants and their legal guardian provided their informed consent. The study was conformed to the Declaration of Helsinki, except for registration in a database, and approved by the local ethical review board (Comité d'éthique de la recherche sectoriel en réadaptation et intégration sociale du Centre intégré universitaire de santé et de services sociaux de la Capitale-Nationale (CIUSSS), # 2018-601).

2.4.2 Procedures

First, all participants filled out a questionnaire to document their level of back pain and their frequency of physical activity. For controls, to ascertain that they had no spine deformation, the Adam forward bend test was performed. To prevent non-vestibular information caused by the electrical current, the skin over the mastoid processes was anesthetized with AMETOP cream (tetracaine HCl gel 4%, Smith & Nephew Medical Ltd., Hull, UK). The cream was applied approximately 30 minutes prior to the placement of the electrodes to minimize cutaneous sensations. Before the electrodes placement, the skin was cleaned with alcohol. To attenuate head

motion during the experiment, participants wore a cervical collar (Stifneck®, Select™ Collar, Laerdal Medical, Stavanger, Norway) allowing to maintain their head orientation tilted upward by $\sim 19^\circ$ (Fig. 2-1, D). The head orientation was measured with a smartphone application (Angle Meter, Smart Tool Factory, Google, Mountain View; Samsung Galaxy S9+, Samsung, Seoul). This head orientation is known to optimize the vestibular-evoked postural response along the mediolateral axis (Mian, et al., 2009).

Participants stood in an upright position on a force platform (AMTI, model OPTIMA, Watertown, USA) with their feet 10 cm apart (i.e., intermalleolar distance), arms alongside, and eyes closed. During standing, the most common force acting on the body is the ground reaction force; the vertical and the shear forces along the mediolateral (ML) and anteroposterior (AP) axes. Force signals were filtered using a zero-lag 4th order low-pass Butterworth filter (cut-off frequency 10 Hz). These signals were collected through a digital-to-analog board (model NI PCIe-6531, National Instrument, Austin, USA) at a sampling rate of 4096 Hz. To create a craniocentric vestibular error signal, an electrical stochastic filtered white noise signal (4th order Butterworth filter lowpass at 25 Hz) was delivered to the 8th cranial nerve through electrodes located on the mastoid processes (5 cm², ValuTrobe® X Cloth Neurostimulation Electrodes, Model VTX5050, Axelgaard Manufacturing Co., Ltd., Fallbrook, USA). The stochastic vestibular signals (SVS: frequency spectrum: 0-25 Hz, amplitude ± 3 mA) were generated using MATLAB and were sent to a constant-current stimulator (DS5 stimulator, Digitimer Ltd, Garden City, UK) through the output of the digital-to-analog board. Such SVS spreads signal power over all frequencies between 0 and 25 Hz. We opted to use SVS as it attenuates anticipation, reduces experimental duration, improves signal-to-noise ratio, and allows spectral analysis (Dakin, et al., 2007; Pavlik et al., 1999; Reynolds, 2011). SVS was delivered in three different configurations: A) bipolar left monaural stimulation, B) bipolar binaural stimulation, and C) bipolar monaural right stimulation (Figure 2-1). These experimental conditions were presented in blocks of 5 trials, randomized across participants, and each trial lasted 60 s.

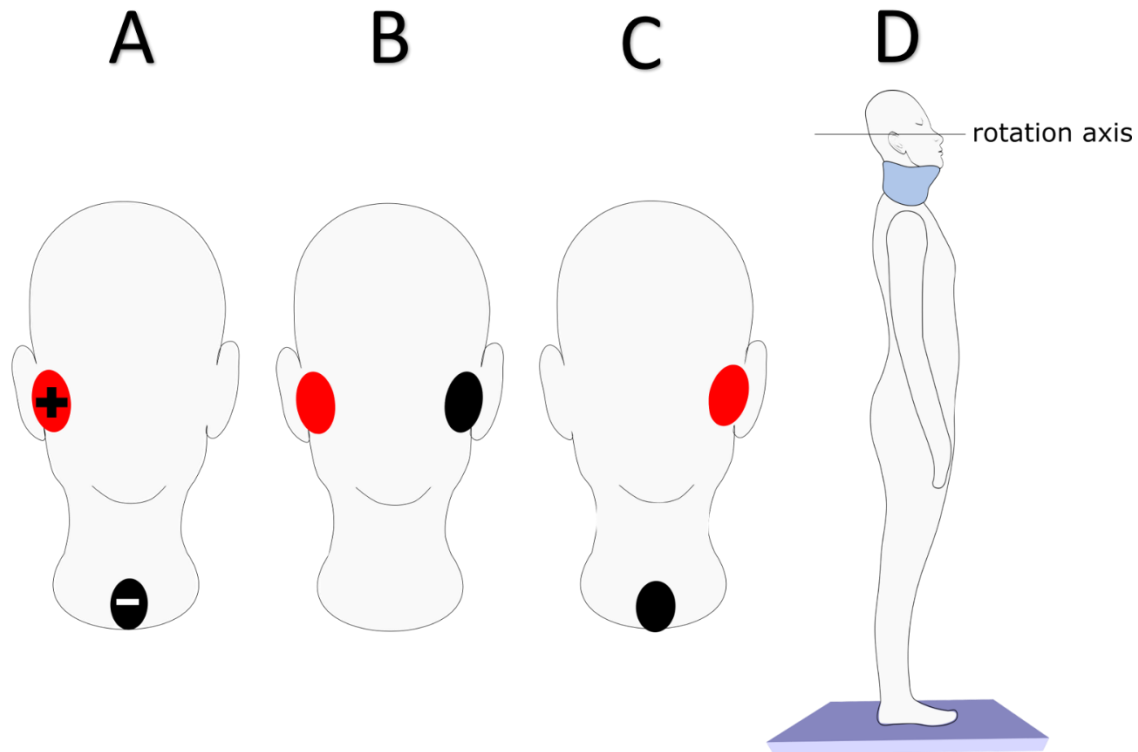


Figure 2-1: Electrodes placement to stimulate the left (A), both (B) or the right (C) vestibular systems. Head orientation to optimize the vestibular-evoked postural response (D).

2.4.3 Data and statistical analysis

2.4.3.1 Coherence, phase, and cross-correlation

Prior to calculating the power spectrum, the force signals were mean-centered and normalized by their root mean square (RMS) values. Group difference in SVS-GRF coherence could relate to difference in power spectra amplitude. Thus, we compared group power spectra by calculating the RMS values between 0 and 10 Hz. Unpaired t-test and paired t-test allowed to verify if the power spectrum differed between groups or during right and left SVS conditions within groups, respectively. To characterize the functioning of the right and left vestibular pathways, we calculated the coherence between the vestibular evoked activity and the GRF signals along the

ML and AP axis. For each group and condition, data from all participants were concatenated to create vectors of SVS and force signals. For the AIS and CTR groups, these vectors were broken down into 2100 disjoint segments and 4500 disjoint segments, respectively. From these concatenated vectors, pooled coherence, phase and cross-correlation between SVS and force signals were calculated with a MATLAB script using functions from the toolbox NeuroSpec 2.0 (Halliday, 2008; Halliday, et al., 1995). Coherence was calculated across all participants as following:

$$C_{xy} = \frac{|G_{xy}(f)|^2}{G_{xx}(f) G_{yy}(f)}$$

Equation 2-1: Equation for coherence.

Where $G_{xy}(f)$ is the cross-spectra between the two signals (i.e., SVS and GRF signals), and $G_{xx}(f)$ and $G_{yy}(f)$ represent the auto-spectra of each signal. Windows of 4096 data points were used to provide a frequency resolution of 1 Hz.

The coherence analysis between SVS and GRF informs about the correlation in the frequency domain between both signals at each frequency. Thus, coherence estimate quantifies the strength and the range of frequencies of common oscillations that are shared between the evoked vestibular signals and the GRF signals. Frequency-specific coherence was significant when the values exceeded the upper limit of the 95% confidence interval derived from the number of disjoint segments used to calculate SVS-GRF coherence. The confidence interval (C) for the coherence estimates was calculated as:

$$CI = 1 - (\alpha)^{\frac{1}{L-1}}$$

Equation 2-2: Equation for the confidence interval.

Where L is the level of confidence (i.e., 95%) and (α) represents the number of disjoint segments (Amjad et al., 1997). To assess the difference between the right and left SVS-GRF coherence, that is to evaluate the functioning of the vestibulospinal pathways, comparison of coherence (CoC) test was performed on pooled coherence for bipolar monaural conditions. The CoC test uses Fisher's transformation (\tan^{-1}) over the coherency values and normalizes the result based on the number of non-overlapping segments. For equal coherence estimates, the null value is zero, whereas values exceeding the 95% confidence interval indicate that the coherence estimate is significant.

Coherence and phase angle are closely related, as the phase between two signals is obtained with the complex valued coherency function, and coherency is the squared root of the absolute value of the coherence (Amjad, et al., 1997; Dakin, et al., 2007). Therefore, to fully appreciate results from pool coherence, it was necessary to calculate the phase angle. We used circular statistics to assess if the phase angle differed between groups. In circular statistics, unlike linear statistics, there is no designated zero. High and low values are arbitrary. For example, two vectors pointing at 359° and 0° have similar directions (Berens, 2009). The Watson-Williams test was chosen to compare the phase angle.

Finally, the inverse Fourier transform of the cross-spectrum allowed to calculate the cross-correlation between SVS and GRF signals. The cross-correlation is a time domain measure informing about the onset (i.e., lag) and the peak of the vestibular-evoked postural response. The positive and negative limits of the confidence interval of the cross-correlation were calculated (Halliday, et al., 1995). Unpaired t-test and paired t-test evaluated the difference in the lag and the amplitude of the peak of the

cross-correlation between AIS and CTR groups or between right and left SVS conditions, respectively.

To explore the relationship between the severity of the spine deformation and the asymmetry in SVS-GRF coherence, for each AIS patient a coefficient of asymmetry was calculated as the RMS value of the CoC test in the 0-10 Hz bandwidth. This frequency bandwidth was chosen since power spectra of the GRF signals and SVS-GRF coherence were higher and showed evident peaks. Pearson's correlation (r^2) between the Cobb angle (main curve) and coefficient of asymmetry was calculated.

2.4.3.2 Norm and orientation of the balance resultant vector

In this study, one aim was to quantify the norm and orientation of the vestibular-evoked postural response. Cross-correlations between the SVS and GRF signals were calculated for all possible directions of postural response. The direction producing the largest correlation value was defined as the postural response direction. Then, the orientation and amplitude of that vector were calculated. More specifically, a referential with a starting direction corresponding to the laboratory ML axis was created and rotated over 360°, with 2° increments. For each rotation, the time series of the components of the force was calculated as following (Mian, et al., 2009):

$$FROT\theta(s) = FLabX(s) \cdot \cos \theta + FLabY(s) \cdot \sin \theta$$

Equation 2-3: Resultant force (FROT(θ)) in function axis rotation (ROT(θ)).

Where $FLabX(s)$ and $FLabY(s)$ represent the time series (s: each sample) of the GRF in the ML and AP axes, respectively, and θ represents the increment of rotation. The peak of the cross-correlation between SVS and FROT θ signals was determined for each increment in a specific window (i.e., 225–500 ms) following lag

zero. This time window was selected because it corresponds to the medium-latency of the vestibular-evoked postural response in the ML direction, known as the principal postural response (Britton et al., 1993). The angle (θ) associated with the cross-correlation peak represented the orientation of the vestibular-evoked postural response.

For each participant, the orientation of the resultant vestibular-evoked postural response was represented on an angular scale. We calculated the mean and standard deviation of the orientation during right and left bipolar monaural SVS conditions. The Watson-Williams test was chosen to compare the orientation of the vestibular-evoked postural responses. To determine if the amplitude of the vestibular-evoked postural response differed between groups for either the right or left SVS condition, we compared the norm of the resultant vector using unpaired t-tests. For all statistical analysis, significance was set at $p < 0.05$.

2.5 Results

2.5.1 Coherence, phase, and cross-correlation

During electrical vestibular stimulation, acceleration of the head towards the cathode is perceived and induces a postural response towards the anode (Fitzpatrick, et al., 2004; Goldberg, et al., 1982). In the present study, we used SVS to probe vestibular information, which allowed to characterize the transfer function between SVS and postural response. Considering the craniocentric nature of the vestibular-evoked postural response, ensuring that the head of the participants was pitched upward at $\sim 19^\circ$ and facing forward optimized the postural response in the ML direction. The power spectrum of the force signals, shown in Figure 2-2, depicts the power amplitude across frequencies for GRF along the ML and AP axis. The magenta and black lines represent the power spectrum for AIS and CTR groups, respectively. Along both axes, power was greater in the 0-4 Hz bandwidth with peak at ~ 1 Hz. The power spectra were similar between groups ($p_s > 0.05$) and between conditions ($p_s > 0.05$).

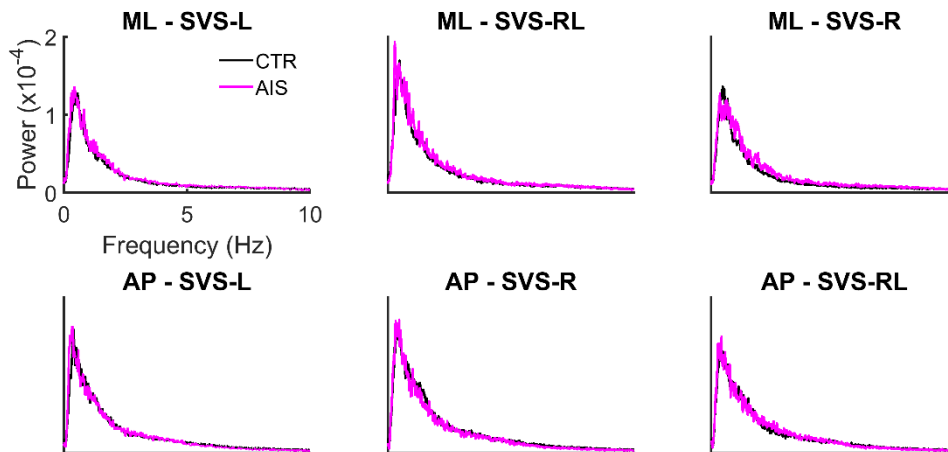


Figure 2-2: Group means for power spectrum of the force signals along the mediolateral (ML: upper row) and anteroposterior (AP: lower row) axes.

One important aim of this study was to compare the right and left functioning of the vestibulospinal pathways. Figure 2-3 shows groups SVS-GRF coherence in the left and right bipolar monaural SVS conditions. The top panels show the coherence estimate for the AIS (magenta line) and for the control (black line) groups during left (left panel) and right (right panel) SVS. Overall, greater coherence was observed in the ML axis, in the 0-12 Hz bandwidth, with peaks below 5 Hz. Coherence estimate revealed significant right and left SVS-GRF coupling in the ML axis for the control group, whereas it was the case only in the right bipolar monaural SVS condition for the AIS patient group. AIS patients did not show significant SVS-ML GRF coupling during left bipolar monaural SVS. For both groups, in the AP axis, the coherence estimate was not significant. The lower panel of Figure 2-3 shows the cross-correlation. The mean amplitude of the peak of the cross correlation was (left monaural SVS: $-6.85 \times 10^{-6} \pm 4.89 \times 10^{-5}$, right monaural SVS: $4.41 \times 10^{-5} \pm 1.69 \times 10^{-5}$) for AIS, and (left monaural SVS: $-3.81 \times 10^{-5} \pm 2.41 \times 10^{-5}$, right monaural SVS: $4.15 \times 10^{-5} \pm 1.97 \times 10^{-5}$) for CTR. For CTR, paired t-test revealed a difference the peak of the cross-correlation between left and right SVS condition ($t(14) = -7.47$, $p < 0.001$), but no difference in AIS ($t(6) = -2.11$, $p > 0.05$). Unpaired t-test revealed no difference between the groups (left: $t(20) = -2.03$, right: $t(20) = -0.31$, $P_s > 0.05$). The mean lag of the peak of the cross correlation was (left monaural SVS: 378 ± 56 , right monaural SVS: 315 ± 72) ms for AIS, and (left monaural SVS: 293 ± 55 , right monaural SVS: 313 ± 57) ms for CTR. Paired t-test revealed a difference the lag of the peak of the cross-correlation between left and right SVS condition ($t(6) = 3.65$, $p = 0.01$) in AIS, but no difference in CTR ($t(14) = -1.17$, $p > 0.05$). Unpaired t-test revealed a delayed lag in AIS compared to CTR during bipolar monaural left SVS ($t(20) = -3.26$, $p = 0.004$).

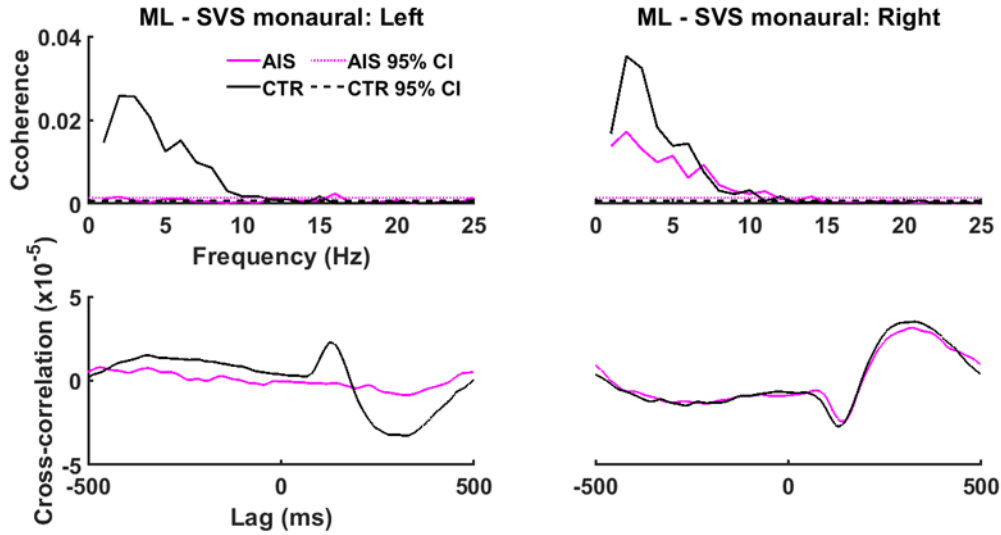


Figure 2-3: Group means for SVS-GRF coherence and cross-correlation for left and right bipolar monaural conditions.

To further investigate the difference in the SVS-GRF coherence, the phase variability between SVS and ML force signals was calculated (Figure 2-4). The variability of the phase is presented for 2 Hz and 5 Hz, since the SVS-GRF coherence at these frequencies were significant across participants. The Watson-William test revealed a difference in the phase angle between the groups during left bipolar monaural SVS (2 Hz: $F(1,20) = 4.87$, $p = 0.03$, 5 Hz: $F(1,20) = 5.05$, $p = 0.04$), but no group difference during right bipolar monaural SVS (2 Hz: $F(1,20) = 0.06$, 5 Hz: $f(1,20) = 0.54$, $ps > 0.05$).

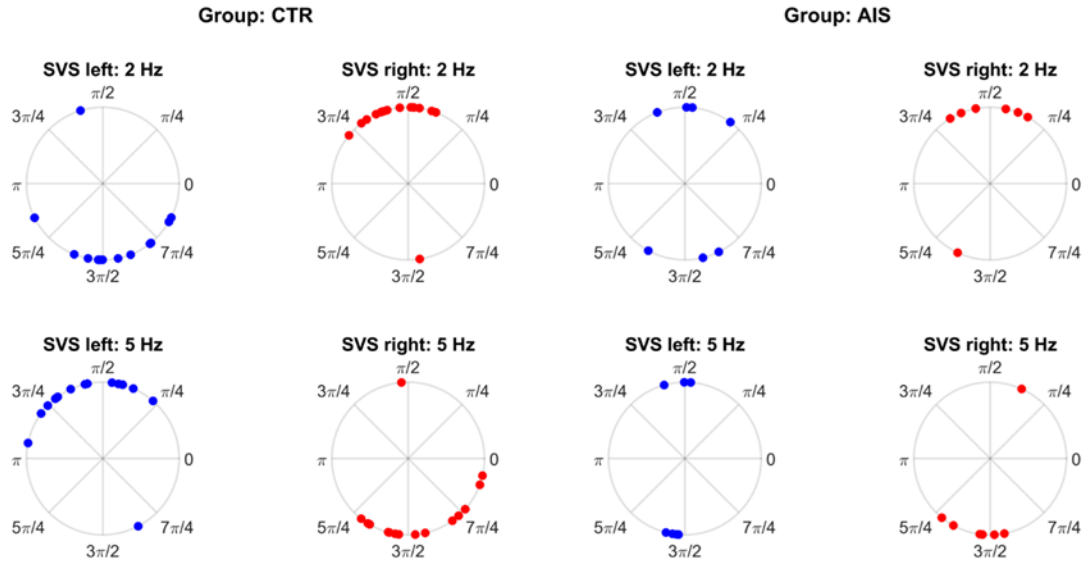


Figure 2-4: Group means for phase at 2 Hz (upper row) and 5 Hz (lower) for left and right bipolar monaural conditions.

For the AIS group, results from the CoC test along the ML axis (Figure 2-5) revealed a significant difference between the right and left SVS-GRF coherence in the 1-10 Hz frequency bandwidth. For the control group, however, there was no asymmetry in SVS-GRF coherence. Further, for both groups, there was no coupling between vestibular-evoked activities and GRF along the AP axis (not shown).

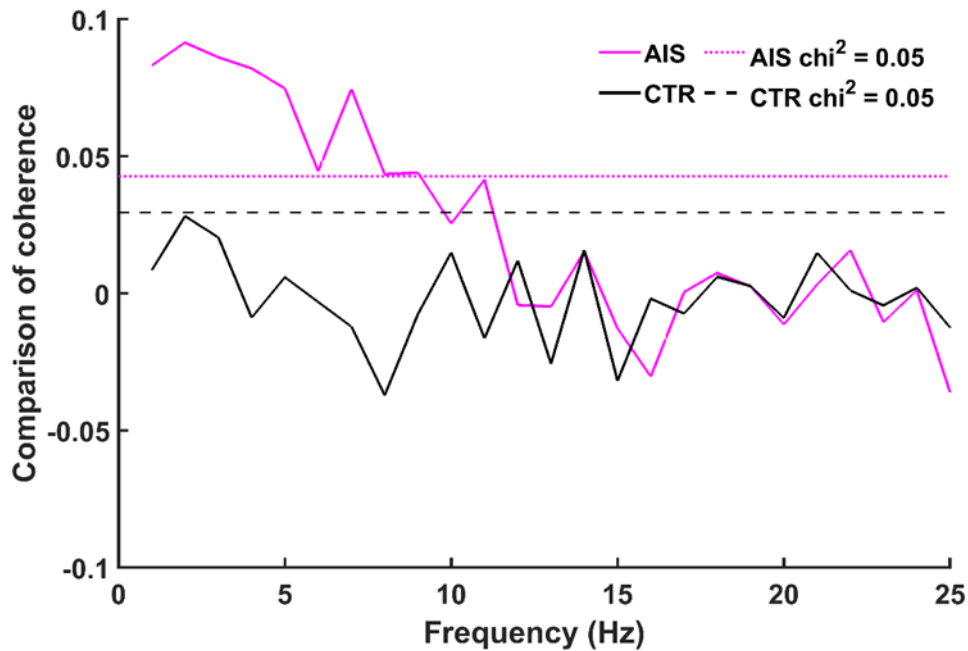


Figure 2-5: Group means for comparison of the right and left SVS-GRF coherence in bipolar monaural conditions.

Results of the spectral analysis of the bipolar binaural condition are shown in Figure 2-6. The top left panel shows the coherence estimate for the AIS (magenta line) and for the control (black line) groups. In both groups, the SVS-GRF coherence revealed significant coupling along the ML axis for the 1-12 Hz frequency bandwidth, with evident peaks below ~5 Hz. Coherence in the AP axis (top right panel) was not significant. The lower panel of Figure 2-6 shows the cross-correlation. Unpaired t-test revealed no difference in the amplitude ($t(20) = 0.40, p > 0.05$) or in the lag ($t(20) = 0.22, p > 0.05$) of the peak of the cross-correlation in the ML axis in AIS compared to CTR.

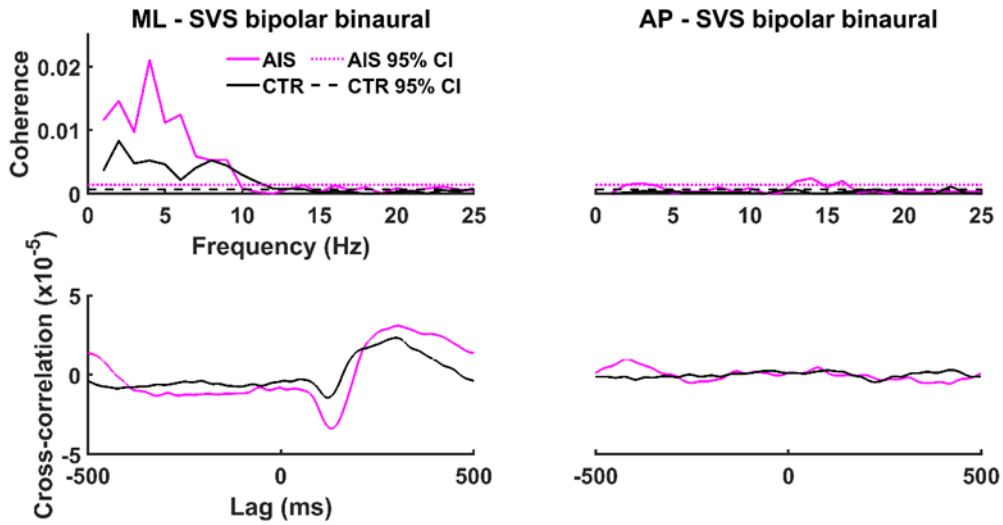


Figure 2-6: Group means for SVS-GRF coherence (upper row) and cross-correlation (lower row) in bipolar binaural condition.

Figure 2-7 shows the relationship between the severity of the spine deformation (i.e., Cobb angle) and the asymmetry in SVS-GRF coherence. Result revealed no association between the SVS-GRF asymmetry and the spine deformation severity ($p = 0.21$, $r^2 = 0.30$).

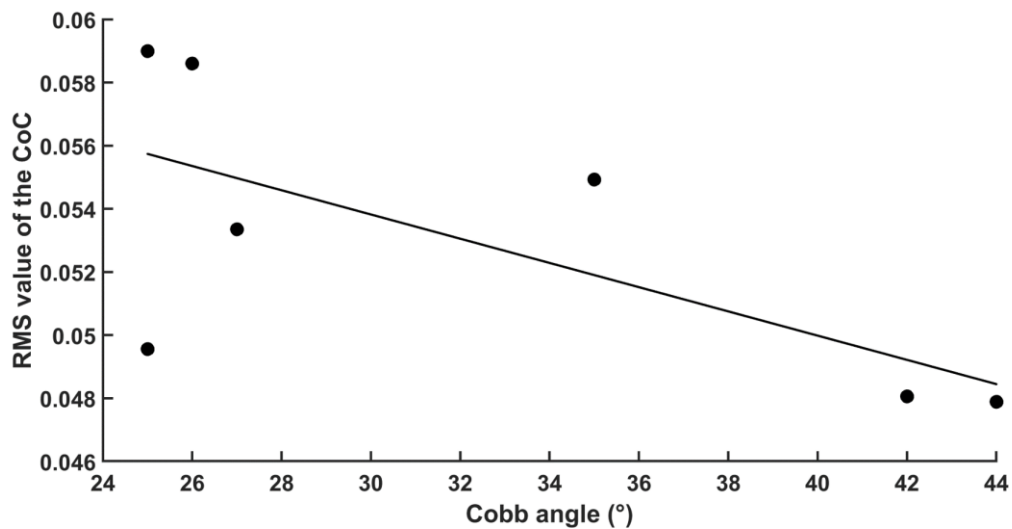


Figure 2-7: Relationship between AIS severity and SVS-GRF coherence asymmetry.

2.5.2 Norm and orientation of the resultant vector

One last aim of the present study was to quantify the norm and the orientation of the vestibular-evoked postural response. The individual resultant postural response vectors, in the bipolar monaural SVS conditions, are depicted in Figure 2-8. The figure depicts mean postural response vectors, viewed from above, for the control (left panel) and the AIS (right panel) groups. The thin arrows represent the individual resultant vectors and the thick arrows show the group means. Red and blue thick vectors represent the resultant vestibular-evoked postural response for right monaural and left monaural SVS, respectively. The mean postural response of the control group was oriented along the ML axis (left monaural SVS: orientation = $179.7 \pm 42.4^\circ$, right monaural SVS: orientation = $24.4 \pm 40.8^\circ$). In the AIS group, the mean resultant vector was oriented (left monaural SVS: orientation = $79.5 \pm 71.5^\circ$, right monaural SVS: orientation = $18.5 \pm 44.9^\circ$). The Watson-William test revealed a difference in orientation of the postural response between the two groups during left bipolar monaural SVS ($F(1,20) = 4.59$, $p = 0.04$). In AIS and control groups, there was a noticeable variability in the orientation of individual response. The norm of the resultant vectors was (AIS: left monaural SVS: norm = 0.31 ± 0.39 N, right monaural SVS: norm = 0.61 ± 0.35 N, CTR: left monaural SVS: norm = 0.57 ± 0.75 N, right monaural SVS: norm = 0.51 ± 0.30 N). Neither unpaired t-test nor paired t-test revealed difference between the groups or between the right and left SVS conditions, respectively ($ps > 0.05$).

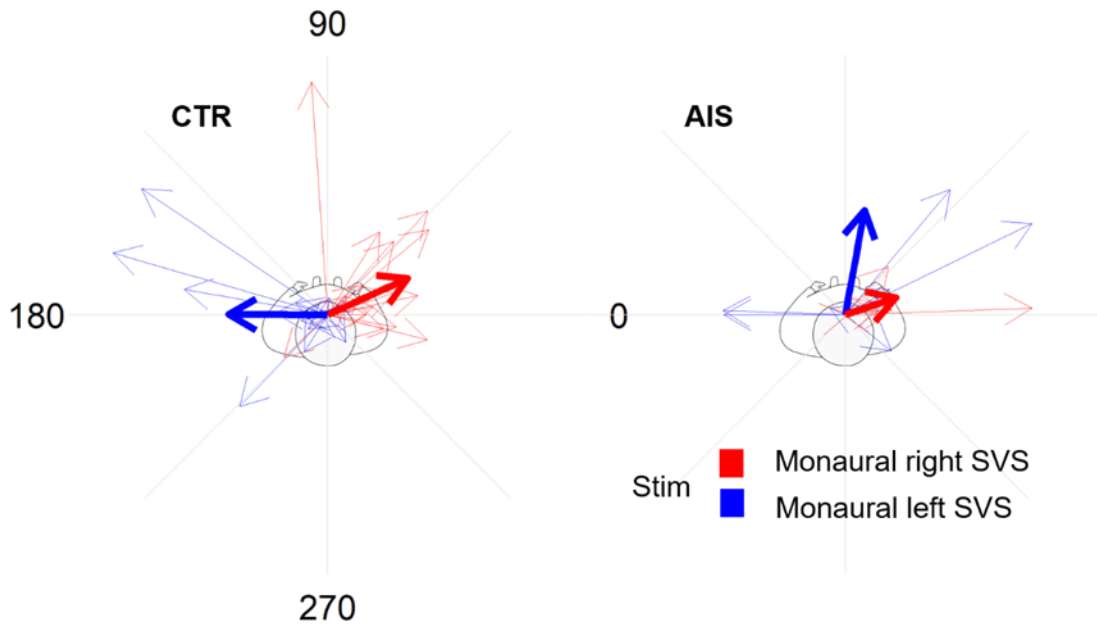


Figure 2-8: Individual norm and orientation of the resultant vector of the vestibular-evoked postural response in bipolar monaural conditions.

Results from the individual resultant vectors of the bipolar binaural SVS evoked balance responses are shown in Figure 2-9. The mean balance response was oriented at 4.1 ° for the control group, and 346.6 ° for the AIS group. The Watson-William test and unpaired t-test revealed no difference in the orientation or the norm between the two groups, respectively ($p_s < 0.05$).

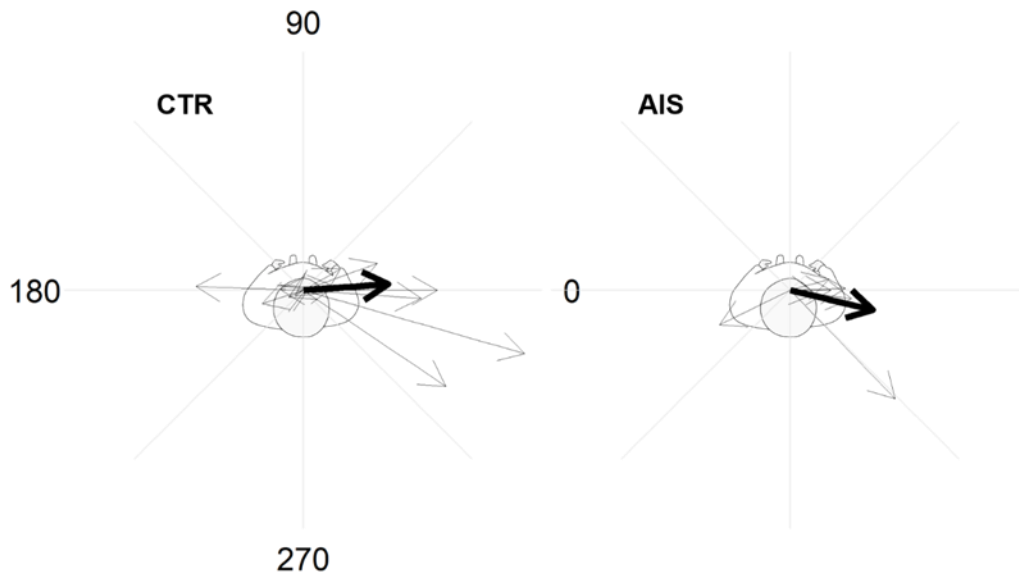


Figure 2-9: Individual norm and orientation of the vestibular-evoked postural response in bipolar binaural condition.

2.6 Discussion

Results from a previous animal study have revealed that asymmetrical vestibular functioning leads to asymmetrical neural drive to the torso muscles and induces spine deformation in *Xenopus* Frog (Lambert, et al., 2009; Lambert, et al., 2013). Further, the processing of vestibular cues is less effective in AIS patients compared to controls (Pialasse, et al., 2015; Pialasse et al., 2017; Sahlstrand, et al., 1979; Simoneau, et al., 2009; Woo, et al., 2019). Thus, the aim of the present study was to assess the functioning of right and left vestibular pathways of adolescents with idiopathic scoliosis, and to compare it to healthy adolescents by calculating the coherence between vestibular evoked activity and postural response. We hypothesized that AIS patients would show asymmetrical functioning of the vestibular pathways. This observation should imply alteration in the transformation of vestibular information into postural response. Consequently, we hypothesized that orientation of the vestibular-evoked postural response of the AIS group, compared to CTR group, would be deviated with respect to the interaural axis. The results confirmed our hypotheses. Asymmetrical SVS-GRF coherence was observed for the AIS group during left bipolar monaural SVS and the orientation of the vestibular-evoked postural response was deviated with respect to the interaural axis. In contrast to our hypothesis, the amplitude of the vestibular-evoked postural response of the AIS group did not differ from the amplitude of the control group. During bipolar binaural SVS, control and AIS groups showed significant SVS-GRF coherence.

2.6.1 Coupling between vestibular-evoked activities and postural responses

Forbes et al. (2013) have proposed that different postural responses to right vs left monaural vestibular stimulation indicates independent processing of vestibular afferents to quantify head acceleration and orientation. In the present study, results of the SVS-GRF coherence during bipolar monaural SVS demonstrated asymmetrical functioning of the vestibular pathways in patients with AIS. It is worth mentioning that asymmetrical coherence does not mean that there was no SVS-GRF

coherence during left monaural SVS. The reduced SVS-GRF coherence during left SVS suggests that among the AIS group, the phase relationship between the SVS and GRF signals was variable. Qualitative analysis confirmed that smaller SVS-GRF coherence during left SVS resulted from greater variability in the phase angle. We could not perform statistical analysis due to the lack of power (i.e., too small number of participants in AIS group). Nonetheless, the attenuated SVS-GRF coherence combined with the delayed lag of the peak of the cross-correlation during left SVS compared to right SVS is a striking result. These observations propose that AIS might be caused by a unilateral alteration in transforming vestibular afferent into proper tonic torso muscles activity.

Although it is crucial to confirm this result by testing more patients with AIS, the greater phase variability and smaller SVS-GRF coherence during left SVS condition can suggest a less efficient coupling between vestibular signals and net motor commands during head accelerations. Using an animal model, it has been demonstrated that unilateral vestibular labyrinthectomy causes an asymmetric motor drive to spinal musculature, leading to a spine deformation (Lambert et al., 2013). Nonetheless, vestibular afferent informs the brain about head accelerations in space, while proprioceptive afferent from neck and torso muscles conveys information about head kinematics with respect to the rest of the body. Several authors have suggested that alteration in muscle spindle might cause spine deformation (Barrack et al., 1988; Ford et al., 1988; Yamada et al., 1984; Yekutieli et al., 1981). Therefore, if muscle spindles and Golgi tendon organs in torso muscles on one side transmit aberrant mechanical sensations to the spinal cord in combination with unilateral alteration in the processing vestibular cues, these conditions would likely favor asymmetric contractions of trunk muscles that may potentially lead to spine deformation during skeletal development.

An intriguing finding was that the reduced SVS-GRF coherence was observed only during left SVS. It is tempting to relate this observation to the direction of the spine deformation, as five out of seven AIS patients had a right thoracic curve as primary curvature. However, scoliosis is a complex spinal deformity. Almost all the AIS

participants in the present study had compensatory curves to the opposite side. It is also worth mentioning that the directions and the amplitudes of spine deformation are not unique, although most of spine deformation is right thoracic (Mellin et al., 1992). In the literature, most of the studies have found no conclusive relationship between spine deformation direction or amplitude and sensorimotor impairment (Pialasse, et al., 2015; Sahlstrand, et al., 1979; Woo, et al., 2019). Even though it is speculative, it is possible that from being stretched for a long time without efferent motor commands, the muscle spindles on the convex side (left torso muscles) added noise within the vestibular-proprioceptive feedback loop causing larger phase variability between SVS and GRF signals.

During bipolar binaural SVS, significant coherence in both groups was noted. This result suggests that while both vestibular systems received SVS, perhaps a central mechanism calibrated the vestibular-evoked activities by subtracting the activities from each vestibular system and eliminating the residual signal. This could ensure proper communication between the vestibular system and postural muscles during bilateral stimulation, as it is during natural head motion. In fact, the proposition of a contralateral vestibular compensation mechanism has been suggested a long time ago (Pfaltz et al., 1973). Vestibular compensation, during binaural vestibular stimulation, has been previously proposed as direction recognition thresholds during bipolar binaural vestibular stimulation and real chair rotations were similar in AIS and controls groups (Woo, et al., 2019). One possible benefit for having two vestibular apparatus is that it offers redundant information leading to lower vestibular information variability. Such central compensation mechanism would provide enhanced vestibular cues to the brain improving perception of the head orientation and acceleration (Day et al., 2010). Such phenomenon could explain to some extent why AIS patients do not present altered balance control in absence of challenging balance control conditions (Byl, et al., 1993).

However, asymmetrical functioning of the vestibular pathways during body growth can alter torso muscle activity and cause spine deformation. Adolescence likely involves a short temporal window during which acute body growth implies sudden

maturation of the sensory systems and body parts. Such event requires rapid and efficient adaptation of the sensorimotor mechanisms. During this period inaccurate coupling between head acceleration and the scaling of torso muscle activity could favor spine deformation. Overall, our results emphasize the importance of using bipolar monaural vestibular stimulation to assess the functioning of the vestibulo-postural response in AIS.

2.6.2 Orientation of the vestibular-evoked postural response

The analysis of the coherence between SVS and GRF along the ML and AP axes allowed to measure the strength in the coupling between vestibular evoked activity and postural response. One limitation of this measure is that it does not inform about the main direction of the postural response. The interest in calculating the norm and orientation of the postural resultant vector was to characterize the direction and amplitude of the vestibular-evoked postural response. It is known that in upright standing position, the vestibular-evoked postural response occurs in the interaural direction (Lund, et al., 1983; Mian, et al., 2009). For the AIS group, during left bipolar monaural SVS, the orientation of the postural response resultant vector was deviated from the interaural direction. One consideration not to be left aside is that bipolar monaural SVS may not activate only the primary vestibular afferents of the stimulation side (Day, et al., 2010; Woo, et al., 2019). Indeed, right and left vestibular stimulation may not purely unilateral, as current could spread and activate the contralateral vestibular afferents resulting in cross stimulation (Aw et al., 2013). But if the orientation of the postural response vector reflected the cross stimulation, similar results should have been observed in both groups and conditions. Altogether, during left SVS condition, the absence of SVS-GRF coherence, the greater variability

in the phase angle, and the deviated postural response point to asymmetrical functioning of the vestibulospinal pathways in AIS.

2.6.3 Assessment of the functioning of the vestibulospinal track

Myelination of the central nervous system in human begins in the fourth month postpartum and is completed around puberty. Myelination, however, does not start in all systems simultaneously, and shows great individual variability (Langworthy, 1932). In the corticospinal tracks, myelination is completed by the age of 2 years. Oscillatory drive, however, emerges later in the development, suggesting that changes in the corticospinal tracks continue into early adolescence (Eyre et al., 1991). Perhaps the development of the vestibulospinal tracks could be similar and not fully attain maturity until early teenage years. Indeed, it has been suggested that vestibulospinal tracks also continue its maturation until at least 12 years of age (Charpiot et al., 2010). In the present study, vestibulo-postural asymmetry cannot be attributed to chronological age difference between the groups. Nonetheless, we do not know if the vestibulospinal tracks follow the same maturation timeline in AIS compared to healthy adolescents.

The vestibulo-postural response likely reflects the functioning of the vestibulospinal tracks, but it could also be influenced by other sensory information (e.g., torso or lower limb proprioception and foot pressor). A protocol using the vestibular evoked myogenic potentials (VEMP) at different levels of the spinal cord could allow for a more extensive assessment of the functioning of the vestibulospinal track in AIS patients. Our results, suggesting vestibulo-postural asymmetries in AIS, leads us to hypothesize that this population could also present VEMP asymmetries.

Confirmation of such hypothesis would allow for a deeper understanding of where originates the vestibulo-postural asymmetry observed in AIS patients.

2.6.4 Limitations

We acknowledge that a limitation of the present study is the sample size of the AIS group. For instance, in the bipolar binaural SVS condition, it was not possible to compare SVS-GRF coherence between AIS and control groups. Indeed, to compare coherence between groups, both groups need to contain the same number of segments (i.e., same number of participants). In the present study, we also wanted to investigate the relationship between the severity of the spine deformation and the asymmetry in vestibulo-postural coherence. Even if more participants are needed in order to increase the statistical power, results of the correlation analysis seem to reveal no association between spine deformation and asymmetry in SVS-GRF coherence. Nonetheless, it seems that the AIS patients with severe spine deformation showed lower SVS-GRF coherence asymmetry. This can appear counterintuitive at first. If vestibulo-postural asymmetry was involved in the onset or in the progression of AIS, one would expect the severity to be positively correlated with SVS-GRF coherence asymmetry. However, participants with moderate scoliosis and large asymmetries in the SVS-GRF coherence could also present greater risks of curve progression. A follow-up longitudinal study would allow to verify whether large asymmetrical SVS-GRF coherence exacerbates spine deformation.

Deficit of vestibular origins, however, is only present in approximately 43-81% of AIS patients (Manzoni et al., 2002; Pialasse, et al., 2017; Wilson, 2013), suggesting that only a subgroup of patients could show sensorimotor alteration (Pialasse, et al., 2017). Moreover, other researchers have tried, without success, to demonstrate an association between the spine deformation severity and sensorimotor dysfunction (Pialasse, et al., 2015; Sahlstrand, et al., 1979; Woo, et al., 2019). Thus, the association between spine deformation and sensorimotor impairment is complex. Obviously, in this study, more participants in the AIS group is needed to investigate

further the relationship between the severity of the spine deformation and SVS-GRF coherence asymmetry.

The present study suggests that SVS-GRF coherence is asymmetrical in AIS patients. The question remains, however, if this observation causes scoliosis or results from the spine deformation (biomechanics hypothesis) and asymmetrical muscle afferences. Nevertheless, the absence of association between SVS-GRF asymmetry and the severity of the spine deformation seems to be in contradiction with the biomechanical hypothesis. Moreover, for the vestibular alteration to be a consequence of AIS, it would be expected that the vestibular system receives direct signals indicating the presence of a spinal deformity or injury (Hawasli, et al., 2015). Complete thoracic spinal cord injury and paraplegia, however, seem to have no effect on the vertical estimate (Barra, et al., 2010; Joassin, et al., 2010). Further, several animal studies have demonstrated that changes in the vestibular system or unilateral sensorimotor cortex ablation causes scoliosis (Domenech et al., 2013; Lambert, et al., 2009; Lambert, et al., 2013). Alteration in balance control, if it was a consequence of the spine deformity, would not be unique to the idiopathic form of scoliosis.

2.7 Conclusion

Scoliosis is a multifactorial disease. Despite the growing evidence for vestibular asymmetries involved in AIS, very few studies have directly assessed the functioning of the right and left vestibular pathways in this population. Results from the present study suggest an asymmetrical functioning of the vestibular pathways in AIS, supporting the suggestion that an error in the processing of the head acceleration can translate into asymmetric motor drive to torso muscles. Therefore, alteration in vestibulo-postural transformation could be involved in the onset or development of the spine deformity. Future studies should investigate if a vestibulo-proprioceptive feedback loop could be related to curve progression.

Chapitre 3 : Discussion générale

La scoliose idiopathique de l'adolescence est une déformation rachidienne commune en orthopédie pédiatrique qui peut avoir des conséquences socioéconomiques et cliniques importantes. À ce jour, les causes d'apparition et de développement de cette déformation du rachis restent mal connues, mais un nombre considérable d'études comportementales, physiologiques et morphologiques suggèrent l'implication du système vestibulaire. L'idée d'un lien de causalité entre une asymétrie vestibulaire et l'apparition de la SIA a été renforcée par des études chez les animaux. Cependant, plus d'études sont nécessaires afin de clairement définir l'implication vestibulo-posturale à l'égard de la SIA. Heureusement, des techniques modernes de stimulation vestibulaire électrique permettent de développer des protocoles et des analyses pour mesurer la qualité de la communication entre le système nerveux central, la moelle épinière et la réponse posturale dans le domaine fréquentiel. Somme toute, déterminer s'il y a un lien entre la présence de SIA et d'une asymétrie vestibulo-posturale pourrait mener au développement de nouvelles techniques de stimulation vestibulaire qui pourraient s'ajouter aux traitements plus conservateurs et ainsi améliorer les conditions de vie des adolescents avec une SIA.

3.1 Sommaire des résultats

Le travail présenté dans ce mémoire de maîtrise avait pour objectif d'évaluer le fonctionnement et l'asymétrie des voies vestibulospinales chez des adolescentes avec une SIA, par l'étude de la réponse vestibulo-posturale lors de stimulations vestibulaires stochastiques bipolaires monaurales (unilatérales) et binaurales (bilatérales). Les résultats qui en découlent suggèrent une asymétrie de cohérence vestibulo-posturale, une plus grande variabilité de la phase, ainsi qu'un délai plus long du pic de la corrélation croisée entre l'activité vestibulaire évoquée et la réponse posturale lors de stimulations de l'appareil vestibulaire à gauche. Ces résultats concordent également avec une asymétrie de l'orientation du vecteur postural

résultant. Les résultats rapportés dans ce travail sont novateurs, puisqu'ils suggèrent que la SIA pourrait être causée par une altération unilatérale de la transformation des afférences vestibulaires en un tonus musculaire asymétrique. Dans l'ensemble, ce travail appuie l'hypothèse d'un fonctionnement asymétrique des voies vestibulospinales chez des patientes avec une SIA (Lambert, et al., 2009; Lambert, et al., 2013).

3.2 Couplage entre l'activité vestibulaire évoquée et la réponse posturale

Différentes réponses posturales lors de stimulations bipolaires monaurales indiquent que les accélérations et l'orientation de la tête sont quantifiées par un traitement indépendant des afférences vestibulaires gauches et droites (Forbes et al., 2013). Alors que les afférences vestibulaires codent pour les accélérations de la tête, les afférences proprioceptives des muscles du cou et du tronc transmettent des informations sur la cinématique de la tête par rapport au reste du corps. Les résultats du chapitre 2 suggèrent un couplage vestibulo-postural moins efficace lors de stimulations vestibulaires unilatérales gauches. Or, une asymétrie vestibulospinale pourrait induire des contractions asymétriques des muscles du tronc. Lors de périodes de croissance rapide, comme à l'adolescence, ces contractions pourraient entraîner une déformation de la colonne vertébrale (Barrack, et al., 1988; Ford, et al., 1988; Yamada, et al., 1984; Yekutieli, et al., 1981).

Mais encore, un résultat intéressant de ce travail est le couplage vestibulo-postural significatif observé chez les adolescentes avec une SIA lors de stimulations vestibulaires bipolaires binaurales. Lors de stimulations binaurales, grâce aux deux appareils vestibulaires, les influx bilatéraux sont combinés. Ainsi, un neurone qui reçoit une excitation d'un canal semi-circulaire reçoit également une inhibition du canal controlatéral complémentaire (Baker, et al., 1984). La redondance de ces informations permet de diminuer la variabilité du signal vestibulaire (Day, et al., 2010). Le système nerveux central détermine alors les accélérations linéaire et angulaire de la tête (Hawasli, et al., 2015). Ainsi, il est possible que lorsque les deux

systèmes vestibulaires sont stimulés, des mécanismes centraux permettent de pondérer l'activité vestibulaire évoquée par la différence entre les activités de chaque système vestibulaire, et la soustraction du signal résiduel. Ceci pourrait refléter un phénomène de compensation vestibulaire lors de stimulations bilatérales, ce qui est toujours le cas lors de mouvements naturels de la tête. Cette idée de compensation est connue depuis longtemps (Pfaltz, et al., 1973), et elle a été observée chez des adolescentes avec un SIA pendant des rotations réelles du corps et lors de stimulations vestibulaires binaurales. En effet, malgré une asymétrie vestibulaire, les adolescentes avec une SIA ont montré un seuil de reconnaissance de la direction de rotation similaire à celui de participants contrôles (Woo, et al., 2019). Ce résultat souligne d'autant plus l'importance d'utiliser des stimulations vestibulaires bipolaires monaurales afin d'étudier l'asymétrie de la réponse vestibulo-posturale, puisque cette asymétrie est atténuée lors de stimulations bipolaires binaurales.

3.3 Orientation de la réponse posturale

En position debout, il est connu que la réponse posturale à une stimulation vestibulaire se produit selon l'axe intéaural, soit environ perpendiculaire à l'orientation de la tête. Or les résultats du chapitre 2 montrent bien que lors des stimulations bipolaires monaurales gauches, les adolescentes avec une scoliose ont une réponse posturale déviée par rapport à l'axe intéaural. Un tel résultat pourrait être causé par une stimulation croisée. Une stimulation croisée se produit lorsqu'une déviation du courant active aussi les afférences vestibulaires contralatérales (Aw et al., 2013). Ainsi, la stimulation n'est peut-être pas purement unilatérale. Or, si les résultats obtenus découlaient d'un tel phénomène, il est raisonnable de penser que l'orientation de la réponse posturale serait aussi déviée chez les adolescentes du groupe contrôle ou encore dans les autres conditions de stimulation, ce que nos résultats ne montrent pas. Ensemble, l'absence de cohérence vestibulo-posturale, la plus grande variabilité de l'angle de phase et la réponse posturale déviée lors de stimulations vestibulaires bipolaires monaurales gauches supportent l'hypothèse

d'un fonctionnement asymétrique des voies vestibulospinales chez les adolescentes avec une SIA.

3.4 Perspectives

Au meilleur de nos connaissances, très peu d'études ont directement adressé l'asymétrie des voies vestibulospinales chez des adolescentes avec une SIA, bien que cette idée ne date pas d'hier (Herman, et al., 1985; Sahlstrand, et al., 1979). Simple, rapide et abordable, le potentiel d'applications d'un test clinique de la réponse vestibulo-posturale chez des adolescentes avec une SIA est pourtant bien réel. De plus, un dépistage précoce d'une asymétrie dans le fonctionnement des voies vestibulospinales pourrait mener à des essais cliniques afin d'évaluer l'efficacité de techniques de stimulation visant à atténuer ou éliminer l'asymétrie fonctionnelle. À long terme, de tels travaux pourraient permettre de diminuer le risque d'apparition ou de progression de la déformation du rachis. Cependant, des questions demeurent concernant l'asymétrie de la réponse vestibulo-posturale observée.

D'abord, l'importance ou la direction de l'asymétrie vestibulo-posturale pourraient être liées à la sévérité ou à l'orientation (droite vs gauche) de la scoliose. Dans le présent travail, nous avons tenté d'explorer ce lien, mais la scoliose étant une déformation complexe, unique à chaque individu, et comprenant souvent des courbes compensatoires, il est difficile de tirer des conclusions générales avec les résultats obtenus. De plus, tel que rapporté dans le chapitre 2, le nombre de participantes du groupe SIA ne permet pas de vérifier de telles hypothèses à l'aide de mesures statistiques suffisamment puissantes. Or, il importe de mentionner et de comprendre le contexte exceptionnel dans lequel s'inscrit la rédaction de ce mémoire. En effet, la crise sanitaire mondiale de la maladie à coronavirus (COVID-19) a forcé l'interruption des collectes de données en laboratoire, et de ce fait la complétion du groupe clinique. Cependant, dès qu'il sera possible, les collectes de données reprendront, et nous serons en mesure de recruter davantage de patientes avec une SIA. La complétion de ce groupe permettra idéalement d'atteindre une

puissance statistique suffisante pour explorer la relation entre l'asymétrie vestibulo-posturale et la sévérité de la SIA.

Dans le présent travail, la réponse vestibulo-posturale a été étudiée uniquement chez des individus de sexe féminin. Un tel choix est justifié par la prévalence plus importante des filles pour la SIA, et aussi parce que la SIA touche plus sévèrement les filles que les garçons (Konieczny et al., 2013; Miller et al., 2001). Mais la présence possible de différences entre les sexes quant au fonctionnement sensorimoteur n'est pas à exclure. Dans un avenir rapproché, nous avons l'intention d'élaborer des protocoles adressant le fonctionnement des voies vestibulospinales des adolescentes et des adolescents avec une SIA, afin d'étudier si la réponse vestibulo-posturale diffère entre les jeunes filles et garçons. Aussi, il serait intéressant de reconduire l'étude de l'asymétrie vestibulo-posturale chez différents groupes d'âge (enfants, adolescents et adultes) afin de vérifier si le développement des voies vestibulospinales est différent chez des individus avec une SIA comparativement aux groupes contrôles.

Il est possible que l'asymétrie de la réponse vestibulo-posturale chez des adolescentes avec une SIA soit le reflet d'un fonctionnement asymétrique de la voie vestibulospinale, mais elle pourrait également impliquer une asymétrie d'autres voies neurales. En effet, les voies corticospinale et réticulospinale constituent aussi des voies descendantes majeures qui ont des projections convergentes aux motoneurons et interneurons spinaux. Par exemple, des auteurs ont aussi mesuré une asymétrie de l'activité corticale chez des participantes avec une SIA, ce qui suggère également un fonctionnement asymétrique de la voie corticospinale chez cette population (Fortin, et al., 2019). Cette récente découverte, combinée aux résultats du présent document, supporte l'hypothèse qu'une asymétrie des voies descendantes serait liée à la SIA. D'une part, les mesures de l'activité corticale, à l'aide d'un électroencéphalogramme (EEG) et de l'activité musculaire, à l'aide d'un électromyogramme (EMG), lors de contractions isométriques des extenseurs du dos (muscles paraspinaux) ou des extenseurs de la cheville (muscles gastrocnémiens) permettraient l'étude de la cohérence, du gain et de la phase corticomusculaire, et

ainsi d'étudier le fonctionnement de la voie corticospinale. D'autre part, le fonctionnement de la voie réticulospinale pourrait être étudié à l'aide du réflexe de sursaut acoustique. Lorsqu'il n'est pas anticipé, un signal auditif crée un réflexe de sursaut, véhiculé par la voie réticulospinale (Yeomans et al., 2002). Une asymétrie de la cohérence intermusculaire lors du réflexe de sursaut, chez les adolescents avec une SIA, indiquerait aussi un fonctionnement asymétrique de la voie réticulospinale.

Conclusion

Bien que la scoliose idiopathique de l'adolescence soit la déformation rachidienne la plus fréquente en pédiatrie, et malgré ses conséquences sur la vie des individus et le risque de progression, ses causes d'apparition et de progression sont encore trop peu connues. Un lien entre une asymétrie sensorimotrice et la SIA est cependant de plus en plus évident. L'objectif de ce mémoire était d'évaluer le fonctionnement et l'asymétrie des voies vestibulospinales chez des adolescentes avec une SIA, en analysant la réponse vestibulo-posturale lors de stimulations vestibulaires stochastiques bipolaires monaurales et binaurales. Les résultats suggèrent une asymétrie vestibulo-posturale chez des adolescentes avec une SIA comparativement à des adolescentes contrôles. En plus d'être novateurs, ces résultats ouvrent la voie pour étudier davantage l'asymétrie des voies neurales descendantes, ou encore étudier l'effet du développement ou du sexe. Dans une perspective clinique, le dépistage précoce d'une asymétrie des voies descendantes pourrait mener à des essais cliniques de techniques de stimulation visant à atténuer ou éliminer l'asymétrie fonctionnelle, diminuant le risque d'apparition ou de progression de la déformation du rachis. Finalement, les nouvelles connaissances générées pourraient permettre de mieux comprendre les mécanismes responsables de la SIA, et possiblement de développer des traitements mieux ciblés, améliorant ainsi la qualité de vie des patientes.

Annexe A : Balance control mechanisms do not benefit from successive stimulation of different sensory systems.

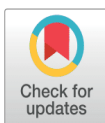
RESEARCH ARTICLE

Balance control mechanisms do not benefit from successive stimulation of different sensory systems

Jean-Philippe Cyr^{1,2}, Noémie Anctil^{1,2}, Martin Simoneau^{1,2*}

1 Département de kinésiologie, Faculté de médecine, Université Laval, Québec, Québec, Canada, **2** Centre interdisciplinaire de recherche en réadaptation et intégration sociale (CIRRISS) du CIUSSS de la Capitale Nationale, Québec, Québec, Canada

* martin.simoneau@kin.ulaval.ca



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Abstract

In humans, to reduce deviations from a perfect upright position, information from various sensory cues is combined and continuously weighted based on its reliability. Combining noisy sensory information to produce a coherent and accurate estimate of body sway is a central problem in human balance control. In this study, we first compared the ability of the sensorimotor control mechanisms to deal with altered ankle proprioception or vestibular information (i.e., the single sensory condition). Then, we evaluated whether successive stimulation of difference sensory systems (e.g., Achilles tendon vibration followed by electrical vestibular stimulation, or vice versa) produced a greater alteration of balance control (i.e., the mix sensory condition). Electrical vestibular stimulation (head turned ~90°) and Achilles tendon vibration induced backward body sways. We calculated the root mean square value of the scalar distance between the center of pressure and the center of gravity as well as the time needed to regain balance (i.e., stabilization time). Furthermore, the peak ground reaction force along the anteroposterior axis, immediately following stimulation offset, was determined to compare the balance destabilization across the different conditions. In single conditions, during vestibular or Achilles tendon vibration, no difference in balance control was observed. When sensory information returned to normal, balance control was worse following Achilles tendon vibration. Compared to that of the single sensory condition, successive stimulation of different sensory systems (i.e., mix conditions) increased stabilization time. Overall, the present results reveal that single and successive sensory stimulation challenges the sensorimotor control mechanisms differently.

Introduction

Human upright balance is inherently unstable. To reduce the small deviations from a perfect upright body position, information from proprioceptive, vestibular and visual systems are combined [1–4]. These sensory signals are continuously reweighted based on their reliability and specificity to maintain the upright standing position [5–7]. To assess the role of each

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sensory cue, it is common to experimentally induce sensory illusions. Electrical vestibular stimulation (EVS) with the cathode electrode located on the right mastoid and the anode electrode located on the left mastoid induces an increase in the firing rate of the right vestibular nerve (cathode) and a decrease in the firing rate of the left vestibular nerve (anode), leading to a body sway towards the anode [8, 9]. Ankle tendon vibrations also induce body sway resulting from the activation of the primary endings of muscle spindles [10]. When vibration is applied to the Achilles tendon, the firing rates of the gastrocnemius and soleus muscle spindles increase (i.e., as if these muscles stretched), suggesting a forward body sway. To counterbalance this illusion, the body sways backward [11]. Previous results suggest that vestibular stimulation influences the processing of somatosensory signals [12–14]. Moreover, human neuroimaging studies have revealed vestibular projections in the primary and secondary somatosensory cortex [15, 16] and the primary motor cortex and premotor cortex [16–18]. The overlap in brain activation of the vestibular and somatosensory inputs is not simply anatomical but also reflects a functional crossmodal perceptual interaction. Psychophysical studies have revealed that vestibular stimulation facilitates the detection of cutaneous stimuli, suggesting a vestibular-somatosensory perceptual interaction [12]. Consequently, it is possible that successive stimulation of these two senses improves balance control.

The first aim of this study was to compare the ability of the sensorimotor mechanisms to control balance during alterations in vestibular information or ankle proprioception. A mathematical model was used to assess the effects of sensory and motor noise on balance control; the results indicate that the magnitude of noise in the vestibular system is ~10 times greater than that of noise in the proprioceptive system [19]. Furthermore, balance control mainly relies on ankle proprioception [20, 21], and its contribution represents more than 60% of balance control [22–25]. Thus, we hypothesize that body sway should be larger during Achilles tendon vibration compared to EVS.

The second aim of this study was to assess whether successive stimulation of different sensory systems alters the performance of the sensorimotor integration mechanisms. During upright standing, a sudden alteration in one sensory information source normally leads to an increase in body sway. When a sensory stimulation is repeated over time, however, the amplitude of body sway decreases [4, 26, 27]. During simultaneous sensory stimulation, the attenuation of body sway is limited or it not necessarily transferred to other senses or other muscles during ankle tendons vibration [26, 28]. It is unclear, however, whether the sensorimotor integration mechanisms can benefit from successive stimulation of different sensory modalities. To address the second aim, we compared balance control performance to a condition in which a single sensory system was altered to a condition in which different sensory systems were stimulated in a chronological sequence. An increase in body sway following the subsequent stimulation would suggest that the error signal from different senses alters the performance of the sensorimotor integration mechanisms.

Materials and methods

Participants

Thirty-two participants (16 men, 16 women, age = 23.1 ± 4.5 years, weight = 69.0 ± 13.2 kg, height = 168.6 ± 10.7 cm) with no known history of neurological or vestibular dysfunction took part in two separate experiments (16 participants in each experiment). Prior to participation, participants provided written informed consent. The study was approved by the Biomedical research Ethics Committee at Laval University (approval number: 2015–119) and conformed to the Declaration of Helsinki standards.

Experimental set-up and protocol

Participants stood barefoot on a force platform (model Optima, Advanced Mechanical Technology, Inc., Watertown, MA, USA) with their feet parallel at 10 cm inter-malleoli and their arms alongside. Their eyes were closed, and their head was turned left at approximately 90° and extended approximately 18°. This head orientation parallels the EVS-evoked rotational vector with the horizontal, thus maximizing the balance response to EVS along the anteroposterior (AP) axis [29, 30]. The force platform signals were sampled at 1000 Hz using a 16-bit A/D converter (model NI PCIe-6531, National Instrument, Austin, TX, USA).

During standing, the most common force acting on the body is the ground reaction force (GRF). It has a vertical and two shear components. The shear forces result from anteroposterior (AP) and mediolateral (ML) directions of the body sway [31, 32]. AP GRF indicates a shift in the sway of the body in the AP direction, and is necessary to prevent a fall. Walking on a slippery surface illustrates this, as in the absence of GRF, the foot slides [32]. In this study, the center of pressure (COP) displacements along the ML and AP axes were calculated from the reaction forces and moments of the force platform. All data were filtered using a zero-lag 4th order low-pass Butterworth filter (cut-off frequency 10 Hz). The center of gravity (COG) along the AP axis was estimated using a zero-point-to-zero-point double integration technique [33, 34] with the assumption that the COP coincides with the vertical line passing through the COM when the horizontal ground reaction force is zero.

Experimental conditions

Applying vibration to a muscle tendon specifically activates the primary endings of the muscle spindle [10, 35]. In this study, vibration ($n = 2$, Freq.: 70 Hz, amplitude: ~1 mm) was applied to the Achilles tendon to cause a backward body sway, which is known as a vibration-induced postural response [11, 36, 37]. Vestibular stimulation was delivered by applying electrical stimulation to the eighth cranial nerve (i.e., vestibulocochlear). Electrical vestibular stimulation (EVS) activates all the primary afferents of the semicircular canals and otoliths, with a cathodal current increasing the firing rate of the afferent and an anodal current decreasing the firing rate [9, 38]. EVS induces a net equivalent motion vector (EVS vector) based on the vectorial summation of all the activated vestibular afferents [8]. According to this model, EVS applied bilaterally over the mastoid processes (i.e., in a binaural bipolar configuration) results in a net rotation around a vector pointing posteriorly and ~18.8° above Reid's plane [39, 40]. Thus, altering the firing rate of the vestibular afferent results in a perceptual illusion of a tilt of falling towards the cathode electrode. To counter this vestibular illusion, muscles are activated creating body sway toward the anode, that is, a backward body sway in the present experiment. To induce vestibular stimulation, a binaural EVS was delivered from a constant-current stimulator (Model DS-5, Digitimer Ltd., Hertfordshire, UK) to electrodes (5 cm², ValuTrode® X Cloth Neurostimulation Electrodes, Model VTX5050, Axelgaard Manufacturing Co., Ltd., Fallbrook, CA) located over both mastoid processes and stabilized with a headband. The stimulus was a 1 mA current step that lasted 5 s (see the explanation of the conditions below).

Throughout the two experiments, we alternated the sequence of sensory stimulation. In both experiments, there were two conditions: single and mix. Under the single sensory condition, sensory information from one sensory system was altered, whereas under the mix sensory condition, information from the two sensory systems was altered in sequence. Thus, during the first experiment, under the single sensory condition (Fig 1A) Achilles tendon vibration created a backward body sway. This condition served as a basis of comparison with the mix sensory condition. Under the mix condition, information from the vestibular and proprioceptive systems was altered in sequence.

For the second experiment (Fig 1B), different participants were involved. Experiment 2 was like experiment 1, but under the single sensory condition, the vestibular apparatus was stimulated first to create a backward body sway. Then, under the mix sensory condition, the Achilles tendon was vibrated after the vestibular apparatus was stimulated. Trials under the single condition lasted for 20 s and were divided into three different epochs: prestimulation (5 s), stimulation (5 s) and poststimulation (10 s). Under the mix sensory condition, trials lasted for 40 s and contained six epochs: prestimulation (10 s), first stimulation (5 s), post first stimulation (5 s), prestimulation (5 s), second stimulation (5 s), and post second stimulation (10 s). Participants performed, in blocks, 10 trials of each of the two conditions.

Data analysis

Balance control performance was assessed by calculating the scalar distance between the time series of the COP and COG displacements (Fig 2A) and then calculating the root mean square (RMS) value of the COP-COG scalar distance in each interval. This measure reflects the linear acceleration of the COM, an indicator of balance control performance [41, 42]. We also calculated the stabilization time, which was the time needed to recover balance when sensory information returned to normal (i.e., poststimulation interval). We considered that balance was recovered when the COP-COG scalar distance was below a defined threshold for 500 ms consecutively. For each participant, the threshold was defined as the mean of the RMS value of the COP-COG scalar distance during the prestimulation intervals (dashed line in Fig 2B).

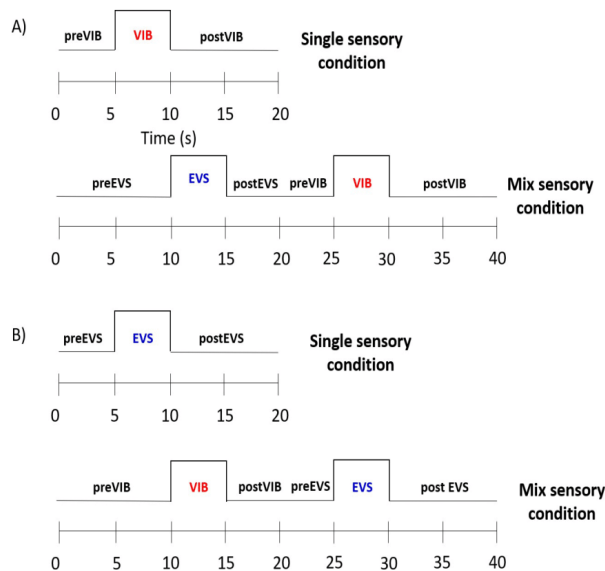


Fig 1. Temporal sequencing of the epochs for both experiments. (A) Time course of experiment 1 that contained two experimental conditions: single and mix sensory conditions. Under the single sensory condition, electrical vestibular stimulation (EVS) was applied to induce backward body sway. There were three epochs: preEVS (0–5 s), EVS (5–10 s) and postEVS (10–20 s). Under the mix sensory condition, Achilles tendon vibration (VIB) was applied first to create a backward body sway. Then, EVS was applied. (B) The time course of experiment 2, which also contained two experimental conditions: single and mix sensory conditions. The epoch durations were as in Experiment 1, but under the single sensory condition, the Achilles tendons were vibrated to create a backward body sway. Under the mix sensory condition, first an electrical vestibular stimulation was applied and then the Achilles tendons were vibrated.

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Furthermore, we determined the amplitude of balance destabilization immediately following sensory stimulation by identifying the peak force along the AP axis (Fig 2C). Visual inspection of every time series showed that peaks occurred at less than 1.5 s following the stimulation offset. Comparison of the peaks between conditions allowed us to verify whether balance destabilization differed when vestibular and ankle proprioception returned to normal.

Statistical analysis

To compare balance control under the single sensory conditions, the RMS values of the COP-COG scalar distance were submitted to analysis of variance (ANOVA) with repeated measures on the factors epoch (prestimulation, stimulation and poststimulation) and condition (VIB, EVS). To contrast balance control performance under the single and mix sensory conditions, the RMS values of the COP-COG scalar distance between the single and mix sensory stimulation were compared through separate ANOVAs with repeated measures on two factors (condition: single, mix; epoch: prestimulation, stimulation and poststimulation). Post-hoc analyses were realized using Tukey's honest significant difference (HSD) test. To assess whether the stabilization time differed between the single and mix conditions, paired t-tests were performed. We evaluated whether balance destabilization (i.e., peak force along the AP axis, following stimulation offset) differed among the single conditions using unpaired T-tests. To compare balance destabilization between the single and mix conditions, paired T-tests were used.

Results

Comparison of single sensory conditions

The results of the analysis of the RMS value of the COP-COG scalar distance (Fig 3) during single sensory stimulation partly confirmed our hypothesis, suggesting that balance control

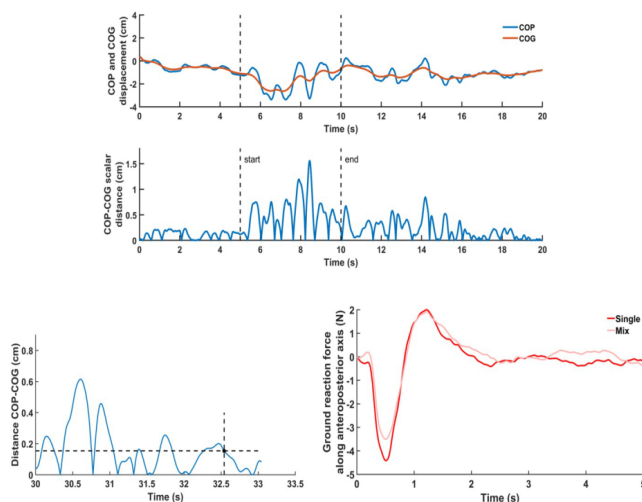


Fig 2. Illustration of the dependent variables. (A) Representative time series of the center of pressure (COP) and center of mass (COM) displacements along the anteroposterior axis. Time-series of the corresponding COP-COG scalar difference. (B) Determination of the stabilization time following sensory alteration. The blue line represents the time series of the COP-COG scalar distance, the horizontal black dashed line represents the stability threshold and the crossing vertical black line with the dot depicts the time when the COP-COG scalar distance is below the stability threshold for the next 0.5 s. (C) Mean time-series of the ground reaction force along the anteroposterior axis following Achilles tendon offset for the single and mix conditions.

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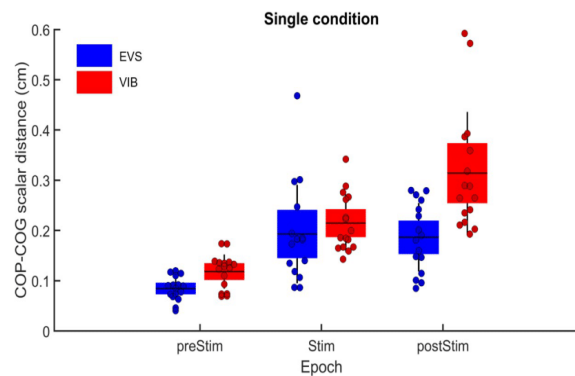


Fig 3. Single sensory condition: Effect of sensory stimulation on balance control. Group means of RMS values of the COP-COG scalar distance before (preSTIM), during (STIM) and after (postSTIM) electrical vestibular stimulation and Achilles tendon vibration under the single sensory condition. The dots depict the mean results for each participant. The horizontal lines illustrate the group means, the boxes denote the group standard error of the mean and the lines depict one standard deviation. The blue data and boxes are for the electrical vestibular stimulation (EVS) condition, and the red data and boxes are for the Achilles tendon vibration (VIB) condition.

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should be poorer when ankle proprioception is altered compared to EVS (significant interaction of Epoch by Condition: $F(2,60) = 6.82$, $p = 0.002$). Decomposition of the interaction revealed that balance control was similar before and during the alterations in vestibular or ankle proprioceptive signals ($ps > 0.05$). When sensory information returned to normal, however, as hypothesized, the RMS value of the COP-COG scalar distance was greater following Achilles tendon vibration ($p = 0.009$). Balance control worsened across epochs (main effect of epoch: $F(2,60) = 47.19$, $p = 0.000$). The RMS value of the COP-COG scalar distance increased from the prestimulation to stimulation epochs ($p = 0.0001$) and from the stimulation to post-stimulation epochs ($p = 0.01$). Overall, balance control performance was worse in VIB compared to EVS conditions (main effect of condition: $F(1,30) = 9.78$, $p = 0.004$).

Balance destabilization under the single sensory condition

Analysis of the peak force along the AP axis revealed that balance destabilization was larger when ankle proprioception returned to normal (mean = -6.24 , $sd = 22.95$) compared to when vestibular information returned to normal (mean = -3.15 , $sd = 1.52$; $t(30) = 3.71$, $p = 0.0008$).

Comparison of the mix sensory conditions

Comparison of the single to mix conditions when vestibular signals were altered (Fig 4A) revealed worse balance control under the mix compared to single conditions (main effect of condition: $F(1,15) = 6.94$, $p = 0.02$). Furthermore, balance control differed across epochs (main effect of epoch: $F(2,30) = 31.94$, $p = 0.000$). During and following EVS, balance control was similar ($p = 0.98$); however, the RMS values of the COP-COG scalar distance in these epochs were greater than in the preEVS epoch. The analysis reported no difference in balance control performance between conditions across epochs (interaction condition by epoch: $F(2,30) = 1.74$, $p = 0.19$). Comparison of the single to mix sensory conditions when ankle proprioception was altered (Fig 4B) revealed no difference (main effect of condition: $F(1,15) = 0.05$, $p = 0.81$). Across epochs, however, the RMS value of the COP-COG scalar distance varied (main effect of epoch: $F(2,30) = 32.19$, $p = 0.000$). Post-hoc tests showed that the RMS value of

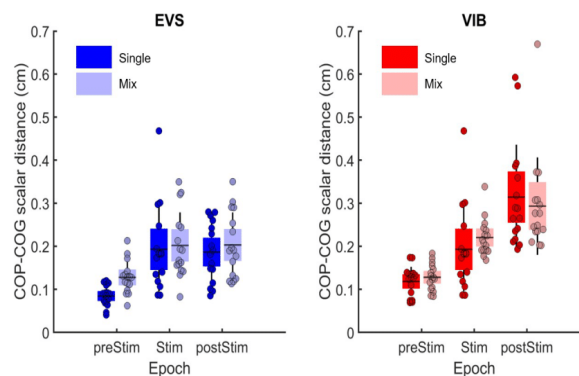


Fig 4. Mix sensory condition: effect of sensory stimulation on balance control. (A) Comparison of the RMS values of the COP-COG scalar distance between single sensory and mix sensory conditions, before (preSTIM), during (STIM) and after (postSTIM) electrical vestibular stimulation (EVS). The blue data and boxes represent the single sensory condition, while the light blue data and boxes depict the mix sensory condition. (B) Comparison of the RMS values of the COP-COG scalar distance between the single sensory and mix sensory conditions for the same epochs for the Achilles tendon vibration (VIB) condition. In each panel, the dots depict the mean results for each participant. The horizontal lines illustrate the group means, the boxes denote the group standard error of the mean and the lines depict one standard deviation. The red data and boxes represent the single sensory condition, while the light red data and boxes depict the mix sensory condition.

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the COP-COG scalar distance increased across epochs (preStim vs Stim, $p < 0.001$ and Stim vs postStim, $p < 0.01$). Across epochs, however, no difference between conditions was observed (interaction condition by epoch: $F(2,30) = 2.53$, $p = 0.09$).

Balance destabilization under the mix sensory condition

The peak forces when vestibular information returned to normal were similar between the single (mean = -3.16 , sd = 1.52) and mix (mean = -3.47 , sd = 1.55 ; $t(15) = 1.14$, $p = 0.27$) conditions. Following Achilles tendon vibration, the peak force did not differ between the single (mean = -6.24 , sd = 2.95) and mix (mean = -5.65 , sd = 2.97 ; $t(15) = -1.84$, $p = 0.09$) conditions.

Time required to reduce the body sway amplitude

Analysis of the stabilization time between the single and the mix sensory conditions revealed that the stabilization time was longer under mix compared to single sensory conditions when either vestibular or ankle proprioception information returned to normal (Fig 5A and Fig 5B: paired T-tests: $t(15) = -4.29$, $p < 0.001$ and $t(15) = -6.86$, $p < 0.001$, respectively).

The RMS of the scalar distance between the COP and the COG approximates the center of mass acceleration. Thus, the fact that the peak forces immediately following sensory stimulation were alike between the single and mix sensory conditions was not surprising as no difference was observed for the RMS value of the COP-COG scalar distance. Balance destabilization (i.e., peak force) immediately following sensory stimulation was a good predictor of the RMS value of the COP-COG scalar distance; the variance explained by the linear model was larger than 80% (Fig 6). Peak force was, however, not a good predictor of the stabilization time (Fig 7) as the variance ranged from 16% to 51%.

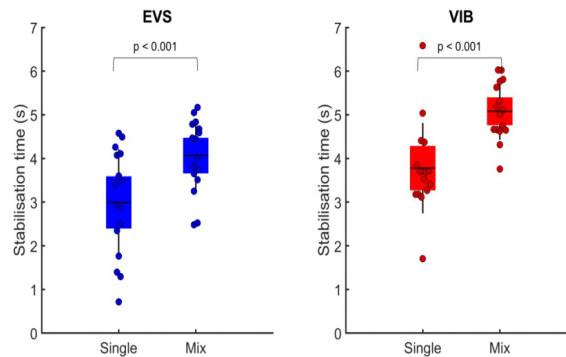


Fig 5. Effect of single versus mix sensory condition on stabilization time. (A) Comparison of the stabilization time following electrical vestibular stimulation (EVS) under the single and mix sensory conditions. (B) Comparison of the stabilization time following Achilles tendon vibration (VIB) under the single and mix sensory conditions. In each panel, the dots depict the mean results for each participant. The horizontal lines illustrate the group means, the boxes denote group standard error of the mean and the blue lines depict one standard deviation.

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Discussion

Not much is known about the time course of sensory reintegration following a sudden change in a sensory state. Rapid and effective sensory reweighting is crucial to alter the balance motor commands and to reduce instability. The aim of the present study was two-fold. First, to compare the ability of the sensorimotor mechanisms to reintegrate ankle proprioception and vestibular cues. Second, to investigate whether successive stimulation of different sensory systems altered balance control performance. Contrary to our hypothesis, the results revealed no difference in balance control performance when ankle proprioception or vestibular information was altered. As expected, however, when sensory information returned to normal, balance control performance was poorer during the reintegration of ankle proprioception compared to

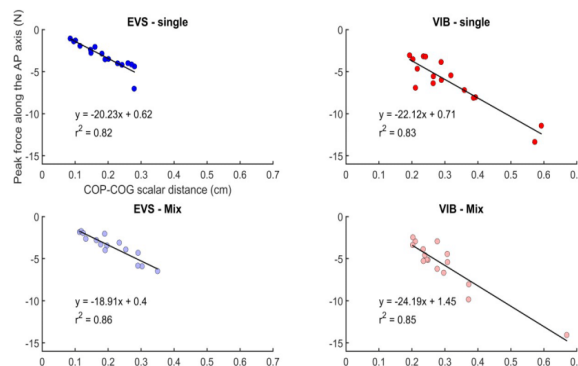


Fig 6. Relationship between balance destabilization and control when sensory information returned to normal. Linear relationship between the peak forces and RMS values of the COP-COG scalar distance for the single (upper left panel) and mix sensory conditions (lower left panel) when vestibular information returned to normal (i.e., post stimulation epoch). Linear relationship between peak forces and RMS values of the COP-COG scalar distance for the single (upper left panel) and mix sensory conditions (lower left panel) when ankle proprioception returned to normal (i.e., post stimulation epoch).

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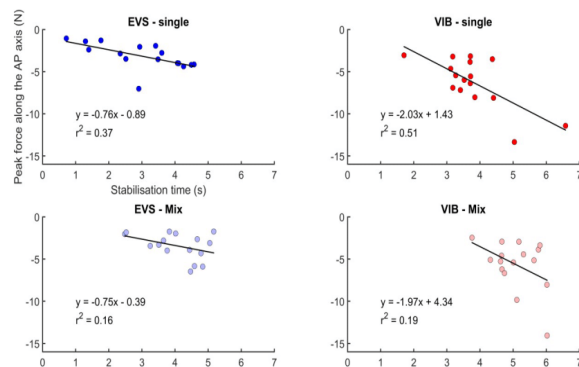


Fig 7. Relationship between balance destabilization and stabilization time when sensory information returned to normal. Linear relationship between the peak force and stabilization time for the single (upper left panel) and mix sensory conditions (lower left panel) when vestibular information returned to normal (i.e., poststimulation epoch). Linear relationship between the peak force and stabilization time for the single (upper right panel) and mix sensory conditions (lower right panel) when ankle proprioception returned to normal (i.e., poststimulation epoch).

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vestibular information. This difference was caused by a larger peak of the ground reaction force, that is, balance destabilization, following Achilles tendon vibration offset. Following successive changes in the sensory state (i.e., the mix sensory condition), the amplitude of body sway did not differ between the single and mix conditions, but the time needed to recover balance was longer under the mix condition.

Comparison of the single sensory conditions

Under the single sensory condition, contrary to our hypothesis, balance control performance was similar during ankle proprioception and vestibular alteration. Poorer balance control performance during Achilles tendon stimulation was expected as balance control mainly relies on ankle proprioception [22–25] and the vestibular system is approximately 10 times noisier than the proprioceptive system [19]. We reasoned that during ankle proprioception alterations in the absence of vision, participants would assign larger weights to vestibular information. Since vestibular sensory information is noisy, this should cause poorer balance control. The absence of a difference between ankle proprioception and vestibular alteration may be due to biomechanical constraints. During this stimulation epoch, the amplitude of the backward body sway was restricted by the posterior stability limit. It is tempting to suggest that in the absence of a stability limit, the body sway amplitude could have been larger during Achilles tendon vibration compared to EVS. Furthermore, to reduce balance destabilization during Achilles tendon vibration, it has been suggested that a participant could adopt a forward tilt posture since such a strategy stretches the Achilles tendon and increases ankle stiffness [43]. It is worth noting, however, that the center of mass accelerations (i.e., RMS value of the COP-COG scalar distance) were similar under both conditions, ruling out this latest suggestion. During ankle proprioception alteration, it is possible that proprioceptive information from other lower limb muscles combined with vestibular cues contributed to improving the state estimates of body sway. This multisensory process likely reduces the overall variance within noisy sensory systems, attenuating body sway [44], which could explain why balance control performance was not poorer during Achilles tendon vibration compared to EVS. However, it is unclear why balance control performance was not better during EVS. Under this condition, unaltered ankle

proprioception could sense body sways, leading to better balance control. One explanation could be that the fusion of ankle proprioception with altered vestibular information led to a noisy unified perception of body sway dynamics and inaccurate state estimation.

When sensory information returned to normal, balance control performance was poorer following Achilles tendon vibration than following EVS. This observation suggests that vestibular reweighting, contrary to ankle proprioception reweighting, could mainly occur at the subcortical level. The vestibular system differs from the proprioceptive system in many ways. First, the same neurons receiving direct afferent inputs can send direct projections to motoneurons, and the first stage of central processing is multimodal [45]. In addition, the vestibular system unambiguously senses head acceleration. Thus, changes in the firing rate of vestibular nerves necessarily provide information about self-motion [46]. By contrast, ankle proprioception either signals the whole-body orientation with respect to the feet or the orientation of the feet with respect to the shin. During ankle dorsiflexion, the brain must determine whether the body sways forward, or the feet are tilted upward. These two situations require balance responses that are fundamentally different, and therefore, such processes should imply complex interactions between cortical and subcortical structures [47–49]. This complex interaction likely causes a slower reweighting. Studies assessing the long-stretch reflexes in lower limbs, due to unexpected surface translation, have reported that these responses are mediated in part by cortical mechanisms [48, 50, 51]. Furthermore, the similarity of the postural responses when different muscles are vibrated means that the motor responses are not caused by the tonic vibration reflex. On the contrary, cortical processing of afferences from all body segments from the feet to the head allows a coherent perception of the whole-body state to be built [52, 53], which is supported by the fact that postural responses, during muscle vibration, are altered by various factors, such as the availability of other sensory cues or balance stability [54–58]. Thus, we suggest that when ankle proprioception returns to normal, the brain must assess the reliability of proprioception, primarily at the cortical level. During the processing of accurate cues, the sum of sensory weight could be transiently larger than one [59]. The slow adjustment of the ankle proprioception weight likely led to an improper corrective ankle torque and therefore a larger center of mass acceleration, which was confirmed by the larger peak force following Achilles tendon vibration offset. Despite the difference between the center of mass acceleration (i.e., RMS value of the scalar distance between the COP and COG) between both single sensory conditions, the similar stabilization time suggests that immediately after Achilles tendon vibration, the balance motor commands were effective in reducing the center of mass acceleration.

Comparison of the single versus mix sensory conditions

In humans, when the vestibular and proprioceptive systems are simultaneously probed, the amplitude of body sway corresponds to the sum of body sway evoked by the stimulation of the two systems alone [14], and multiple muscle co-vibration does not represent a linear summation of the combined effects [52]. Moreover, neuroimaging studies have found vestibular projections in the primary and secondary somatosensory cortices [15, 16] and the primary motor cortex and premotor cortex [16–18]. Psychophysical studies have revealed that vestibular stimulation facilitates the detection of cutaneous stimuli, suggesting a vestibular-somatosensory perceptual interaction [12]. Thus, there is growing evidence for a functional crossmodal perceptual interaction between vestibular stimulation and the processing of somatosensory inputs. Altering ankle proprioception before stimulating the vestibular system could enhance the sensorimotor mechanisms.

Under the mix sensory conditions, the increase in stabilization time suggests that the sensorimotor mechanisms did not benefit from successive stimulation of different sensory systems. The results of the center of mass acceleration (i.e., RMS value of the COP-COM scalar distance) mitigate the latest affirmation. Nonetheless, it is important to distinguish the RMS value of the COP-COM scalar distance from the stabilization time. The RMS value of the COP-COG scalar distance was calculated over a time window and provided information about the amplitude of the center of mass acceleration. The stabilization time represents a discrete event and provides about the time needed to recover a baseline-like balance control performance. Balance destabilization (i.e., peak force) was a good predictor of the RMS value of the COP-COG scalar distance (variance explained $> 80\%$), while it was not a good predictor of the stabilization time (range of variance explained: 16%–51%). These results suggest that these parameters convey different information about the performance of the sensorimotor control mechanisms.

A limitation of the mix sensory conditions was the delay between sensory stimulations. Previous studies have assessed how ankle proprioception and vestibular information interact with each other when altered simultaneously [14, 60]. The direction and amplitude of body sway during ankle proprioception alterations are influenced by simultaneous changes in the vestibular input. In our study, the aim was to verify whether successive stimulation of two sensory systems involved in balance control could be beneficial for the sensorimotor mechanisms. We added a delay of 5 s between sensory stimulations to avoid a transient effect of the previous stimulation on the following stimulation. Furthermore, the delay needed to be short enough to assure that sensorimotor information was shared over time. Neural responses are improved when different sensory cues are temporally and spatially congruent [61–63]. EVS and Achilles tendon vibration evoked body sways in the same direction. However, it seems that the short delay between sensory stimulation prevented a balance control improvement.

Conclusion

Understanding how the brain combines sensory information to quickly adapt its motor commands to sudden changes in sensory states represents a challenge. In the present study, when ankle proprioception returned to normal, the peak of ground reaction force was larger, leading to a faster body sway (i.e., a larger RMS value of the COP-COG scalar distance). However, even though balance control mainly relies on ankle proprioception [22–25], balance control performance did not differ during alterations of ankle proprioception and vestibular information. Moreover, successive alterations of different sensory systems (i.e., mix sensory condition) worsen balance control performance as the time needed to recover balance is longer compared to that under the single sensory condition. The amplitude of the center of mass acceleration and the time required to regain balance control seem to convey complementary information about the performance of the sensorimotor control mechanisms.

Author Contributions

Conceptualization: Jean-Philippe Cyr, Noémie Anctil, Martin Simoneau.

Data curation: Jean-Philippe Cyr, Noémie Anctil.

Formal analysis: Jean-Philippe Cyr, Noémie Anctil, Martin Simoneau.

Funding acquisition: Martin Simoneau.

Methodology: Jean-Philippe Cyr, Martin Simoneau.

Project administration: Martin Simoneau.

Resources: Martin Simoneau.

Software: Jean-Philippe Cyr, Noémie Anctil, Martin Simoneau.

Supervision: Martin Simoneau.

Writing – original draft: Jean-Philippe Cyr, Martin Simoneau.

Writing – review & editing: Martin Simoneau.

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