# Description

The aim of this research project is to investigate in the healthy subject the two-dimensional (2D) or three-dimensional (3D) nature of spatial coordinate systems.

In the horizontal dimension, we need a representation of our body in space in order to represent our surrounding in egocentric coordinates usable for motor actions (Rizzolatti et al., 1997). In the vertical dimension, we need an allocentric representation of gravity in order to maintain postural control and perceptual constancy (Dakin & Rosenberg, 2018). Thus, we can both estimate the position and the orientation of a target, with respect to body and gravity, respectively. In other words, target spatial features (position or orientation) are coded in 3D coordinates.

Our research question bears on how the CNS is building these 3D coordinates. Does the CNS achieve independent 2D gravity coordinates and 2D body-in-space coordinates, or does the CNS achieve a 3D coordinate system where gravity and body-in-space coordinates are co-dependent?

This research question is raised by clinical observations. In right-brain damaged (RBD) patients, both body-in-space and gravity coordinates are abnormally biased (Brandt et al., 1994; Molenberghs et al., 2012; Perennou et al., 2008).

In the horizontal dimension, RBD patients show spatial neglect, the inability to react to and orient to stimuli presented in the contralesional hemi-space (Kerkhoff, 2001). One of the traditional manifestation of spatial neglect is the rightward deviation of body-in-space coordinates. When asked to point toward their “straight-ahead”, in darkness, these patients point too much rightward with respect to their objective body midline (Karnath et al., 1994; Schindler et al., 2006). This straight-ahead rightward bias is also observed in the frontal plane, when RBD patients are asked to align a rod, in translation, with their body midline (Rousseaux et al., 2014).

In the vertical dimension, RBD neglect patients show a contralesional bias of gravity representation in the frontal plane (Baier et al., 2012; Brandt et al., 1994; Funk et al., 2010; Kerkhoff, 1999; Kerkhoff & Zoelch, 1998; Yelnik et al., 2002). For example, in the visual vertical task, where one is asked to orient a luminous line in total darkness, neglect patients typically perceived the line as vertical when tilted 3 to 5° leftward (Kerkhoff, 1999). In addition, the magnitude of the contralesional vertical bias is highly correlated with visual neglect severity (Baier et al., 2012; Funk et al., 2010; Kerkhoff, 1999; Yelnik et al., 2002).

These clinical results raise the possibility that biased body-in-space and gravity coordinates observed especially in RBD neglect patients may arise from a common disorder, affecting a represented 3D spatial coordinate system. Alternatively, attention orientation in the horizontal plane and gravity coordinates may be partially co-dependent (Kerkhoff & Zoelch, 1998). Finally, it might be the case that body-in-space and gravity coordinates are strictly independent, relying on different neural networks, yet very close at the anatomical level.

To disentangle these different scenario, our objective is to evaluate in the healthy subject both body-in-space and gravity coordinates before and after an intervention known to bias either body-in-space coordinate or gravity coordinate. If the CNS produces 3D spatial coordinates, then the induction of a body-in-space perception bias should be associated with a gravity perception bias. Reciprocally, the induction of a gravity perception bias should be associated with a body-in-space perception bias. Moreover, if gravity perception and body-in-space perception are co-dependent, then the induced gravity and body-in-space spatial biases should be correlated.

# Hypotheses\*

To test our hypothesis, healthy participants will undergo leftward prism adaptation, a sensori-motor training known to bias straight-ahead (SA) perception rightward (Rossetti et al., 1998). The same subjects will also undergo the virtual tilted-room (VTR) illusion, a paradigm known to bias visual vertical (VV) perception (Odin et al., 2018), here 18° in the counter-clockwise direction. If the CNS produces 3D spatial coordinates, then the induction of a rightward SA after-effect (post-test bias – pre-test bias) should be associated with a leftward VV after-effect, and vice-versa, thus mimicking a pattern of pseudo spatial neglect. Moreover, we don’t expect any significant after-effect on SA and VV with control prism adaptation (plain glasses without optical shift) and control VTR (virtual room aligned with gravity).

Thus, our main prediction is a main effect of the Perturbation independent variable (leftward condition vs. control condition) on both VV after-effects and SA after-effects, in both interventions (prism adaptation and VTR). The novelty of this hypothesis is to predict an effect of prism adaptation on VV, and an effect of VTR on SA, never demonstrated in the literature.

Our secondary hypothesis bears on the linear relationships between the SA and VV after-effects, within and between interventions. Thus, we expect a significant negative correlation between the SA after-effect and the VV after-effect in both prism adaptation and VTR interventions (within-intervention correlation). Moreover, we also expect a significant negative correlation between the SA after-affect induced by VTR and the VV after-effect induced by prism adaptation (between-intervention correlation).

# Study Design\*

SA and VV after-effects will be analysed with a within-subject design, with Perturbation (leftward, control) as within-subject variable.

# Randomization\*

For each participant, the order of the four sessions (prism/control, prism/leftward, VTR/control, VTR/leftward) will be randomly determined. The random number list used to create these sequences will be created using the web applications available at http://random.org (option "Integer Set Generator").

# Statistics\*

If data distribution is Gaussian, both SA and VV after-effects will be analysed with a one-tailed paired t-test with Perturbation (leftward, control) as within-subject variable. Otherwise, SA and VV data will be applied a log transformation (before calculating the after-effect, which can take negative values) to follow a Gaussian distribution. If transformations are inoperative, SA and VV after-effects will be analysed with a non-parametric one-tailed Wilcoxon test (aka Mann-Withney-Wilcoxon test).

To investigate the correlations between the SA and VV after-effects, we will first calculate SA and VV delta scores from the Perturbation conditions (eg., SA leftward – SA control). These delta scores will provide “corrected” after-effect measures, controlled for the after-effect obtained without leftward perturbation. Correlations between these delta SA and VV after-effects will be calculated with Pearson or Spearman correlations, depending on the Gaussian distribution of the data.

# Data exclusion\*

First, the presence of outliers will be check graphically with boxplots. Second, studentized residuals will be examine to check whether one observation has extreme influence (“pulling”) on statistical estimates. By convention, studentized residuals above 4 are considered as highly influent. Analyses will be run with and without outliers (Judd et al., 2017).

# Missingness\*

Missingness (eg, one participant realizes three out of four sessions only) will be handled by using Linear Mixed Model (LMM, aka multilevel model) thanks to the R library “lme4” (Bates et al., 2015). If the LMM doesn’t converge properly, we will estimate statistical parameter with a multilevel Bayesian approach, thanks to the R library “brms” (Bürkner, 2017). Because a Bayesian procedure constrains the model with a priori knowledge (“prior”), statistical parameters can be more easily approximated.

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Finally, we are also interested in the correlation between different types of after-effects. An index of after-effect can be obtained by extracting for each subject his/her [Time X Perturbation] interaction slope value for a given measure.

With this method, we will test the correlations between :

- prism after-effect on SSA AND prism after-effect on VV

- VR after-effect on SSA AND VR after-effect on VV

- VR after-effect on SSA AND prism after-effect on VV

# DRAFT

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1) Hypotheses tested by ANOVA

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According to the "3D hypothesis", the recalibration of the egocentric spatial coordinates in the horizontal plane should recalibrate the gravitocentric spatial coordinates in the frontal plane too, and vice-versa.

First, we expect a significant effect of LPA on both SSA and visual vertical. The SSA after-effect (ie, posttest - pretest) should be oriented rightward, whereas the visual vertical after-effect shoud be oriented leftward.

Second, we expect a significant effect of the virtual reality immersion (leftward tilt) on both SSA and visual vertical. The SSA after-effect (ie, posttest - pretest) should be oriented rightward, whereas the visual vertical after-effect shoud be oriented leftward.

Importantly, we expect that the control conditions (sham prism adaptation and upright virtual reality) shouldn't give rise to significant after-effects on either SSA or visual vertical. To control for this possibility, we will test the interaction between the Condition variable (control vs biased) and the Time variable (pretest vs posttest) for each intervention (prism adaptation and virtual reality). We expect a significant interaction explained by a simple effect of Time in the biased condition but not in the control condition. These simple effects should be directed in the predicted direction, without being necessarily significant. Note that we are particulary interested in the 2x2x2 interaction, because the effects of each intervention on SSA or visual vertical are by no means comparable.

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2) Hypotheses tested by correlations

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The effect of each intervention on the dependent variables will be evaluated by extracting for each individual the interaction slope value between Time and Perturbation. Concretely, this interaction slope indicates the after-effect difference between the control and the deviation conditions. The larger the interaction slope, the larger the deviation condition has biased the SSA or the visual vertical compared to the control condition. Thus, we will assess for each intervention the correlation between the interaction slopes for SSA and those for visual vertical. We aim to examine if participants who showed a "large" interaction in one plane (horizontal or frontal, SSA or visual vertical) showed a "large" deviation in the other plane too.

Finally, we will test whether the two “trans-dimensional” after-effects —effect of prism adaptation on visual vertical; effect of virtual room tilt on SSA— are correlated within the same participants. Indeed, if egocentric and gravitocentric spatial representations rely on the same cognitive process, we expect that a “large” trans-dimensional after-effect in one direction should result in a similar “large” trans-dimensional after-effect in the other direction. To test this hypothesis, we will examine the correlation between two measures : the individual interaction slope values (Perturbation X Time) for the visual vertical in the prism adaptation intervention ; the individual interaction slope values (Perturbation X Time) for the SSA in the virtual reality intervention.

To investigate these hypotheses, we will submit healthy participants to leftward prism adaptation (LPA), a visuo-motor adaptation training known to bias egocentric spatial perception rightward (Prablanc et al., 2020). When the subject is asked to point toward a visual target, prism wearing induces a leftward error pointing. Then the error signal triggers an adaptation process that realigns proprioceptive coordinates of the hand and retinal visual coordinates, in the rightward direction (Bastian, 2008). After prism removal, SSA is usually shifted rightward after LPA, as compared with the pre-test SSA orientation (the so-called "after-effect" [AE]).

According to the "3D hypothesis", the recalibration of the egocentric spatial coordinates in the horizontal plane should recalibrate the gravitocentric spatial coordinates in the frontal plane too. At the operational level, we expect a correlation between rightward after-effects bearing on the SSA, and leftward (counterclockwise) after-effects bearing on the visual vertical tasks. We thus expect to induce a pseudo-neglect in the horizontal plane sided by a pseudo vertical bias in the frontal plane.

Crucially, we will also test the mirrored prediction that a specific intervention known to bias the visual vertical should in turn bias the SSA orientation. In this view, we plan to expose the same healthy participants to a virtual environment tilted 18° leftward in the frontal plane. This paradigm is perfectly suited to bias the visual vertical (Odin et al., 2018; Witkin & Asch, 1948). According to the "3D hypothesis", we should observe a rightward rotation of the SSA after a sustained immersion of the subject (4 minutes) in the virtual tilted room.

Finally, we will test whether the two “trans-dimensional” after-effects —effect of prism adaptation on visual vertical; effect of virtual room tilt on SSA— are correlated within the same participants. Indeed, if egocentric and gravitocentric spatial representations rely on the same cognitive process, we expect that a “large” trans-dimensional after-effect in one direction should result in a similar “large” trans-dimensional after-effect in the other direction.