

Brief Report

Corticospinal Excitability During a Perspective Taking Task as Measured by TMS-induced Motor Evoked Potentials

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Abstract: Only by understanding the ability to take third-person perspective can we begin to elucidate the neural processes responsible for one's inimitable conscious experience. The current study examined differences in hemispheric laterality during a first-person perspective (1PP) and third-person perspective (3PP) taking task, when using Transcranial Magnetic Stimulation (TMS). Participants were asked to take either the 1PP or 3PP when identifying the number of spheres in a virtual scene. During this task, single-pulse TMS was delivered to the motor cortex of both the left and right hemispheres of 10 healthy volunteers. Measures of TMS-induced motor-evoked potentials (MEPs) of the contralateral abductor pollicis brevis (APB) were employed as an indicator of lateralized cortical activation. The data suggest that the right hemisphere is more important in discriminating between 1PP and 3PP. These data add a novel method for determining perspective taking and add to the literature supporting the role of the right hemisphere in meta representation.

Keywords: Perspective Taking; Self-Awareness; Self-Representation; Metarepresentation; Theory of Mind; Transcranial Magnetic Stimulation

Perspective taking is a fundamental aspect of human existence and a likely driver of human brain evolution (Fabbro, Cantone, Feruglio, & Crescentini, 2019; Heyes & Frith, 2014), including the enhancement of aspects of the frontal (Sherwood et al., 2006) and parietal lobes (Patel, Sestieri, & Corbetta, 2019). With the emergence of a variety of imaging techniques, a number of regions have been identified in perspective taking (Heleven & Van Overwalle, 2018; Lamm, Rütgen, & Wagner, 2019; Quesque & Brass, 2019). Across both patients (Dichter, 2012; Vucurovic, Caillies, & Kaladjian, 2020) and experimental studies, converging evidence appears to implicate the Right Temporal Parietal Junction- rTPJ (Dichter, 2012; Patel et al., 2019; Vucurovic et al., 2020) and Medial Prefrontal Cortex- MPFC (Li, Mai, & Liu, 2014; Schurz, Radua, Aichhorn, Richlan, & Perner, 2014; Smith & Lane, 2015) in adopting another person's perspective.

One of the essential features of consciousness is *perspective* (Taylor, 2001; Schilbach et al., 2006). At the most basic level, all mammals possess a first person-perspective (1PP), also termed "central-representation" or "primary representation" (Vogeley, 2004). This is the non-reflexive ability to simply *know* without explicit reflection or meta-representation of any kind. During 1PP, one would not *think*, "I am here", but rather *just be* here (Eilan, 1995). The second person-perspective (2PP) is commonly defined as the ability to monitor one's own mental state in a self-representational capacity, other-

wise known as being *self-aware* (Gallup, 1970; Krachun, Lurz, Mahovetz, & Hopkins 2019). In doing so, one is able to attend to one's own cognitions in a proprietary, self-reflective manner. Differentiating between 1PP and 2PP is dependent upon the ability to actively monitor or mentalize one's thoughts in the past, present, and future (2PP) as opposed to mere present awareness (1PP).

Previous research into the understanding of perspective taking has utilized linguistic paradigms (e.g., Molnar-Szakacs, Uddin, and Iacoboni, 2005; Platek, Myers, Critton, & Gallup, 2003; Platek, 2010; Richardson et al., 2020), self-face paradigms (e.g., Keenan, Wheeler, Gallup, Pacual-Leone, 2000; Liu et al., 2020; Platek, Keenan, Gallup, Mohamed, 2004; Sperry, Zaidel, & Zaidel, 1979; Preilowski et al., 1977; Sugiura, 2014), affective interpretation tasks (e.g., Simon Baron-Cohen, 1996; Rutherford, Baron-Cohen, & Wheelwright, 2002; Golan, Baron-Cohen, Hill & Rutherford, 2006; Eidelman-Rothman et al., 2016), tactile tasks (e.g., Schaefer, Xu, Flor, & Cohen, 2009; Schaefer, Heinze & Rotte, 2012) and lesion studies (e.g., Feinberg & Keenan, 2005; Breen, Caine & Coltheart, 2001; Stuss, Gallup, & Alexander, 2001), using both on-line and off-line approaches (e.g., Perner & Lang, 1999).

Evidence suggests that 2PP and 3PP may recruit similar cortical areas, lending support for an underlying neuroanatomical network that mirrors their applied functional similarity. A number of brain regions have been implicated in these meta-representational functions, including: the right prefrontal cortex (e.g., Keenan et al., 2000; Platek et al., 2003; Feinberg et al., 2005; Tullett, Harmon-Jones & Inzlicht, 2012), parietal regions (e.g., Wolper, Goodbody, Hussain, 1998; Lou, Luber, Crupain, Keenan, Nowak, et al., 2004; Lou, Luber, Stanford & Lisanby, 2010; Taylor, 2001; Northoff & Bermpohl, 2004), the medial prefrontal cortex (MPFC; e.g., Duran et al., 2020; Mitchell, Banaji, & Macrae, 2005; Johnson, Raye, Mitchell, Touryan, Greene & Nolan-Hoeksems, 2002; Gallagher, Happe, Brunswick, Fletcher, Frith, & Frith, 2000; Johnson, Schmitz, Kawahara-Baccus, Rowley, Alexander, Lee, & Davidson, 2005; Vogeley et al. 2001; David et al. 2006; Schilbach et al., 2006; Pfeiffer et al., 2014; Zysset, Huber, Samson, Ferstl, & Yves von Cramon, 2002), orbitofrontal regions (e.g., Berthoz, Armony, Blair & Dolan, 2002; Gregory et al., 2002; Bouc et al., 2012; Sabbagh, 2004) and the posterior cingulate cortex (e.g., Johnson et al., 2002; Kircher et al., 2002; Lou et al., 2010; Oschner et al., 2005).

Of key interest is that although a large body of evidence has examined the link between 2PP and 3PP, very little is known about the contrast between primary-representation (1PP) and that of the meta-representational states of 2PP and 3PP. It is unclear whether 1PP relies on similar or disparate cortical regions as those involved during 3PP and if 1PP is preferentially lateralized in the RH. One way in which 1PP has been successfully studied is through visio-spatial tasks which require the "centering on one's multimodal experiential space upon one's own body, thus operating in an egocentric reference frame" (Vogeley, May, Ritzl, Falkai, Zilles, & Fink, 2004). Vogeley et al. (2004) created a visio-spatial paradigm in which the individual is required to shift between one's own body axis perspective (1PP) and taking another's vantage point as their own (3PP).

1. Motor Evoked Potentials (MEPs)

Transcranial Magnetic Stimulation (TMS) delivered to the 'hand area' of the motor cortex elicits a Motor Evoked Potential (MEP) in the contra-lateral digits (Barker, Jalinous, & Freeston, 1985; Klomjai, Katz, & Lackmy-Vallée, 2015). MEPs have become a part of almost every TMS application as they are used to measure individual differences in motor threshold (MT: Lefaucheur, 2019; Maeda, Keenan, Tormos, Topka, & Pascual-Leone, 2000), and it is generally thought unsafe to use TMS without gauging some aspect of MT (Anand & Hotson, 2002; Groppa et al., 2012; Wassermann et al., 1996; Zis et al., 2019). Since its inception, MEPs have been used for wide-ranging investigations including post-stroke recovery (Kubis, 2016), ALS (Vucic et al., 2018), schizophrenia (Kas-

kie & Ferrarelli, 2018), intrinsic brain rhythm activity (Hanajima & Ugawa, 2019) and even veterinary medicine (Journée et al., 2019).

In terms of perspective taking, a study examined piano players who were presented with music they practiced previously. When they thought the left hand part of the music was being played by another person, the MEPs in the left arm were greater, and MEPs increased as the participant's empathy increased (Novembre, Ticini, Schütz-Bosbach, & Keller, 2012). Further, previous work by our lab demonstrated that adopting another's perspective (e.g., pretending to be a fan of an opposing sports team) led to greater left motor cortex/right hand MEPs (Kelly et al., 2009).

Centered on first-person perspective, a number of researchers employed TMS-induced motor-evoked potentials (MEPs) to measure lateralized cortical excitability during the presentation of self-descriptive adjectives (Molnar-Szakacs, Uddin, & Iacoboni, 2005). The adjectives identified as highly or not at all descriptive of the individual resulted in increased right hemisphere excitability, indicating that the degree of self (including rejecting descriptions of oneself) could be discriminated via MEPs. The amount of one's *self-perception* can alter MEPs such that participants' positivity or sense of personal power results in differing senses of personal space (Vergallito et al., 2019).

Differences in perspective taking that exist in motor areas are not surprising. Lateralized hand response differences (e.g., reaction time and identification) exist such that there is a tendency for left-handed responses to be quicker for self-related stimuli (Keenan, Freund, Hamilton, Ganis, & Pascual-Leone, 2000; Keenan, Ganis, Freund, & Pascual-Leone, 2000; Keenan et al., 1999; Ma & Han, 2010). Furthermore, the handedness of the individual plays a significant role in how self (compared to other) is processed in the brain. While right-handed individuals tend to be more consistent and right-hemisphere dominant for self-processing, left-handed individuals display greater variability (and more left hemisphere involvement) in cortical response (Morita, Asada, & Naito, 2020). Therefore, both the hand that performs the task and an individual's hand dominance influence perspective taking.

In order to further our understanding of the cortical mechanisms involved during 1PP and 3PP, we employed the same task in which participants were presented with virtual scenes of an avatar (i.e., a virtual character) and a number of red spheres (Vogele et al., 2004). Participants were instructed to report how many red balls would be visible either from their own (1PP) or the avatar's perspective (3PP). The current study administered TMS to both the right and left motor cortices (MC) to determine the degree of lateralization during 1PP and 3PP. It was predicted that TMS administration to the right MC would generate larger MEPs during assumption of the avatar's perspective (3PP). This prediction is suggestive of the greater involvement of the RH during Theory of Mind (ToM), lending support to the theoretical, anatomical and cognitive similarity between 2PP and 3PP. The advantage of MEPs over traditional neuroimaging is the direct assay of excitability rather than the possibility that increased signal may be indicating inhibitory firings (Maeda, Keenan, Tormos, Topka, & Pascual-Leone, 2000). Therefore, if difference are found, a more direct interpretation is possible.

2. Materials and Methods

2.1. Participants

Ten right-handed adults (4 men, 6 women) were recruited via flyer and word of mouth from Montclair State University and Seton Hall University (for similar samples, see Brady et al., 2019; Kim et al., 2019; Kumru, Kofler, Valls-Sole, & Vidal, 2019). The mean age of the participants was 22.1 (SD=2.84). Participants were appropriately screened using the TMS safety guidelines established by Wasserman (1996, 1998). All subjects received \$25 for participation in the study and were treated in accordance with the standards and guidelines set forth by the Institutional Review Board (IRB) of

Montclair State University. Written informed consent was obtained from all subjects. (IRB code: MSU IRB 424)

2.2. Materials

A TMS-Magstim 200 MonoPulse device with a 70mm figure-8 coil was used to stimulate cortical areas of the brain. Stimuli were presented using SuperLab (Cedrus Corporation, Version 2.01) on a Dell computer with a 17" inch CRT monitor. MEPs were acquired using Biopac MP150 amplifiers and accompanying acquisition software installed on a Dell computer. MEPs were recorded using three surface electrodes attached to areas of the hand, using EC2 electrode paste and surgical tape.

2.3. Procedure

For each subject, three surface electrodes were affixed to both hands, at the abductor pollicis brevis (APB) and the belly-tendon montage. A ground electrode was placed on the back of the wrist. Subjects were fitted with earplugs and a swim cap and then seated in front of a computer monitor with their head in a chin rest, 30 inches away from the computer monitor. Due to individual differences in corticoexcitability, Motor Threshold (MT) was first established. The MT was determined by stimulating the area of the primary motor cortex (M1) responsible for hand movement. The Motor Threshold is achieved by slowly increasing the stimulation intensity until hand movements a) can be visually detected, in the contralateral hand, in 5/10 cortical stimulations (Wasserman, 1996) and b) met the IFCN guideline of MEP's over 50 (Rossini et al., 1994). MT determination was established for both hemispheres, for each subject.

Subjects were then presented with a virtual scene that included an avatar and a varying number (1-3) of red spheres within or out of sight of the avatar (Figure 1). The subjects were asked to determine "how many balls they see" (1PP) or "how many balls the avatar sees" (3PP; Vogeley et al., 2004). The experimenter recorded verbal responses. Single-pulse TMS was administered to the motor cortex of either the left or right hemisphere 150 ms or 300 ms following stimulus presentation onset. All stimulation was delivered at 100% MT due to IRB regulations at MSU which capped TMS at 100%. In each condition and for each hemisphere, 48 trials were presented (left hemisphere, 1PP; left hemisphere, 3PP; right hemisphere, 1PP; and right hemisphere, 3PP; 192 total pulses per individual were given). All stimuli remained on the screen until the participant made a verbal response. Reaction times were not recorded (that is, onset of verbal response time). Trials were separated by an inter-trial-interval (ITI) of 1500 ms between each trial within condition. The left and right hemispheres were stimulated separately with the order of stimulation and conditions counterbalanced across subjects. TMS onset post-stimulus presentation was randomized for each condition.

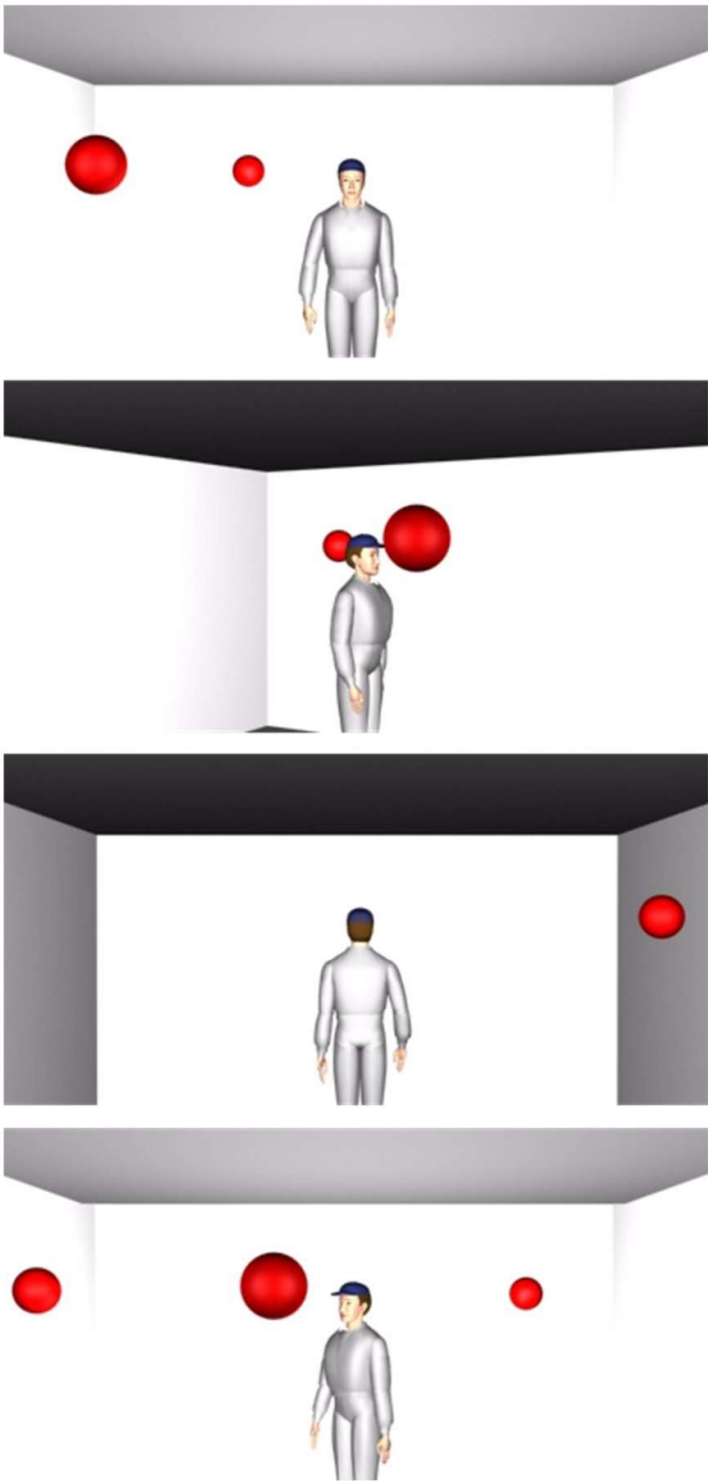


Figure 1. Stimuli of avatar and spherical balls. Each frame presented here demonstrates a different correct response for 1PP and 3PP. Stimuli were adapted from (Guise et al., 2007; Vogeley et al., 2004).

Measures of TMS-induced MEPs of the APB were recorded. The EMG signal was amplified by a factor of 1,000, filtered (bandpass amplifier filter between 1 Hz - 500 Hz), and digitized using a sampling rate of 500 samples per second. All data were stored on a computer for off-line analysis. MEP data were filtered off-line using a Finite Impulse Response (FIR) linear bandpass filter (between 10-250 Hz) employing BIOPAC provided software. The remaining data were then rectified and averaged within-subject by condition. The threshold for data rejection was defined as baseline amplitudes that exceeded 100 μ v. Following data rejection, group means were computed.

3. Results

For each condition (1PP and 3PP), measures of TMS-induced MEPs for grand-averaged data were analyzed in terms of peak amplitude, area under the curve (AUC) and overall variability (SD). We began our analyses by directly testing a number of a priori comparisons. The timing of TMS onset was first analyzed using an independent samples t-test. Across conditions, the TMS pulse onset (150 vs 300 msec) did not impact MEP peak, AUC or variability ($p > .05$). As such, pulse onset was collapsed across all trials and conditions. A 2x2x2 (1PP/3PP; Left/Right Hemisphere Stimulation; 150/300 msec TMS-Onset) repeated measures Analysis of Variance (ANOVA) was performed. In the absence of a 3-way interaction ($F(1,23) = .72$, $p > .05$), a significant interaction between Hemisphere x Perspective was found ($F(1,23) = 6.55$, $p < .02$). The Right Hemisphere x 1PP differed significantly from all other conditions. 1PP, during right hemisphere stimulation, resulted in a significant decrease in peak amplitudes when compared to all other conditions. Additionally, a significant main effect for Perspective was found ($F(1,23) = 5.57$, $p < .05$), in that 1PP yielded less robust peak amplitudes as compared to 3PP (Figure 2). There were no other significant main effects (p 's $> .05$).

Figure 2. The Peak (A), AUC (B) and SD (C) across Hemisphere for 1PP and 3PP. In all 3 measures, the 1PP Right Hemisphere condition differed significantly from all other conditions (all p 's $< .05$). All other comparisons were non-significant. A representative rectified, smoothed MEP is given for the 1PP (D) for RH and LH.

A second repeated-measures ANOVA was calculated to examine AUC differences. There was no significant 3-way interaction ($F(1,23) = .02$, $p > .05$). However, a significant interaction between Hemisphere x Perspective was found ($F(1,23) = 11.63$, $p = .002$). A significant main effect was found for the 1PP/3PP condition ($F(1,23) = 8.029$, $p < .05$), revealing a decrease in MEP AUC during the 1PP condition. A main effect for Hemisphere was also revealed ($F(1,23) = 6.63$, $p < .05$), such that the LH AUC was significantly greater than the RH AUC. The interaction between Hemisphere and Perspective, for both peak amplitude and AUC, indicates decreased right hemisphere activation during 1PP only.

Lateralized differences in MEP variability may offer unique insights into the consistent nature of the cortical response during differing perspectives. We therefore examined differences in SD using ANOVAs. There was no significant 3-way interaction ($F(1,23) = .004$, $p > .05$). There was no interaction between TMS Onset and Hemisphere or TMS Onset and Perspective (p 's $> .05$); however, a significant interaction between Hemisphere and Perspective was found ($F(1,23) = 8.86$, $p < .007$). Using the Bonferroni correction for multiple comparisons, post-hoc analysis revealed that the variability of the self-right hemisphere condition was significantly lower compared to all other conditions (p 's $< .05$). Additionally, a significant main effect for Perspective was found ($F(1,23) = 11.66$, $p < .002$), such that the self-condition was less variable than the other-condition. Main effects for Hemisphere and TMS onset were not found (p 's $> .05$).

4. Discussion

The current study sought to identify lateralized differences during first- and third-person perspective-taking. These data revealed significant differences within the RH for perspective taking. Both peak amplitude and AUC differed significantly between perspectives within the RH. No such differences were observed in the LH. An MEP reduction (for both amplitude and AUC) was noted for the RH during primary-representation, indicating that 1PP may require less activation in the RH. While it is not surprising to see a general decrease in MEP measures from 3PP to 1PP, as a function of task difficulty, the RH is considered to be dominant in spatial processing. In keeping with this, the LH did not evidence a decrease in MEP measures across perspectives.

The question remains: if meta-representational abilities of 1PP and 3PP seem to be lateralized in the RH, why was no significant difference in corticoexcitability between hemispheres during the 3PP condition found? There are a few possible explanations. First, although not significant, the RH did produce larger peak amplitudes than the LH during 3PP. However, the AUC measures were more similar. This may suggest inherent differences in MEP latency and length. As such, some studies indicate that the analysis of the MEP silent period (PMSP; Pascual-Leone, Bartres-Faz & Keenan, 1999) may provide an alternate means of interpretation. However, these analyses were not possible with the data we collected, because our MEP recordings were not long enough to capture the inhibitory response (i.e., typically 300 ms). Furthermore, there is some evidence to suggest that the left motor cortex produces a greater MEP response as a function of greater activation of the left motor cortex in general (Pascual-Leone, Bartres-Faz & Keenan, 1999).

Previously (Théoret, Kobayashi, Merabet, Wagner & Tormos, Pascual-Leone, 2004), an increase in MEPs were found for self-related processing. While one can describe the difference in results through task dissimilarity, a further explanation may be provided by a paper on Alexithymia (Moriguchi et al., 2006). Using functional magnetic resonance imaging (fMRI) during a perspective taking task, researchers found that the Alexithymic group demonstrated greater activation in the RH compared to the non-Alexithymic group, though performance was superior for the non-Alexithymic group. Furthermore, and perhaps critical, is that activation in the right superior parietal cortex in the Alexithymic group increased as a function of symptom severity. Therefore, it is possible that reduced MEPs may indicate a region is particularly adept or specialized at processing stimuli. As we have previously reported (Kelly, Murray, Barrios, Gorman, Ganis & Keenan, 2009), during a linguistic processing task, we found reductions in cortical activation during ToM tasks as ToM ability increases. Therefore, the possibility is likely more than speculative (Kobayashi, Glover & Temple, 2008).

Because much research has indicated regions such as the MPFC (e.g., Courtney & Meyer, 2020; D'Argembeau, Feyers, Majerus, Collette, Van der Linden, et al., 2008; Kedia et al., 2019; Lieberman, 2007; Molnar-Szakacs, Uddin, Zaidel, Iacoboni, 2007; Oschner, Beer, Robertson, Cooper, Gabrieli, et al., 2005; Lou, Luber, Crupain, Keenan, Nowak, et al., 2004; Seger, Stone & Keenan, 2004; Schilbach, Ritzl, Krämer, Newen, Zilles, et al., 2006; Zhao et al., 2016) as critical for self/other differentiation, this study is limited in its scope. However, the current study further supports lateralized findings by demonstrating that self/other discriminations are significantly different between the hemispheres. These data add to a growing amount of evidence that the RH appears critical in evaluating self/other differences, tested across a number of different modalities in non-patient (e.g., Keenan, Nelson, O'Connor & Pascual-Leone, 2001; Keenan, Wheeler, Platek, Lardi & Lassonde, 2003; Kotlewska & Nowicka, 2015; Morita, Asada, & Naito, 2020; Morita et al., 2008; Naito et al., 2017; Sugiura, Miyauchi, Kotozaki, Akimoto & Nozawa, et al., 2014; Uddin, Molnar-Szakacs, Zaidel & Iacoboni, 2007; Prencipe & Zelazo, 2005) and patient populations (e.g., Candini et al., 2018; Delgado & Bogousslavsky, 2018; Dieguez, 2018; Feinberg & Keenan, 2005; Frassinetti et al., 2012; Frassinetti, Maini, Romualdi, Galante, & Avanzi, 2008). Decety and Lamm (2007) have suggested that superior right parietal processing

may be critical for both switching and differentiating self/other distinctions. Our current data support this possibility.

An underused measure of MEPs has been variability between responses, and here we show that the right MC has less variability in response. While it remains unclear what this may mean, we suggest that intuitively reduced variability may indicate increased efficiency. Typically, MEP variability is looked at in terms of either population differences (Richter, Ehrlis, Jacob & Fallgatter, 2007) or physiological changes (Darling, Wolf & Butler, 2006). We suspect that a further use may be in terms of efficiency, though we admit this is speculative. We believe that testing other paradigms; in particular those that simulate 'real-life' situations (Klichowski & Kroliczak, 2020) such as knowing what another driver sees vs. what one sees would be a valuable line of investigation. Future studies should also examine the associate priming (Werner, von Ramin, Spruyt, & Rothermund, 2018) and we believe that a well-designed study could tease out both (the ecological significance and the degree of semantic or associative priming the two tasks have).

Further, our participant number could be increased in future studies. Likewise, additional measures of 1pp and 3pp should be collected in future studies.

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