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Harnessing the Brain's Neuro-Compensatory Processes: Lessons from a High-Functioning Person with Complete Agenesis of the Corpus Callosum

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It remains elusive how and why some people born with profound brain structure abnormalities develop high levels of intellect and near normal behaviour, while others with what appears to be the same or similar structural abnormalities experience far more concerning phenotypical outcomes. To begin to address this issue, a high-functioning female (aged 17 years at testing) born with complete callosal agenesis (ACC1) was tested on a series of psychophysical tests requiring unimanual-sequential or bimanual object weight discrimination; the latter of which is believed to depend on the integrity of the corpus callosum. In all five variants of the weight-discrimination task, ACC1's performance was well within two standard deviations of the sample distribution mean. Arguably within the normal range, her performance warrants further investigation. Results suggest that individuals like ACC1 hold the secret to future understanding of the elusive neuro-compensatory processes of the human brain.

Keywords: corpus callosum, agenesis, weight discrimination, neuroplasticity, bimanual actions

Il demeure difficile d'expliquer comment et pourquoi certaines personnes nées avec des anomalies structurelles cérébrales profondes développent des niveaux d'intellect supérieurs et des comportements dans la norme, alors que d'autres, présentant des anomalies structurelles identiques ou similaires, subissent des impacts préoccupants. Pour explorer cette problématique, une participante hautement fonctionnelle de 17 ans, née avec une agénésie du corps calleux complète (ACC1), a été évaluée à l'aide d'une série de tests psychophysiques impliquant une discrimination séquentielle à une ou deux mains du poids d'un objet, cette dernière considérée dépendante de l'intégrité du corps calleux. Pour les cinq étapes de la tâche de discrimination, la performance d'ACC1 était à moins de deux écarts types par rapport à la moyenne de l'échantillon. Sa performance dans la normale illustre la nécessité d'études supplémentaires. Les résultats indiquent que les individus comme ACC1 détiennent le secret d'une meilleure compréhension du processus neuro-compensatoire du cerveau humain.

Mots clé : corps calleux, agénésie, discrimination de poids, neuroplasticité, actions bimanuelles

The human brain is a highly neuroplastic system formed through complex interactions between genes and environment, with adaptive changes occurring throughout development. Neuroplasticity describes the anatomical and functional adaptability of the brain. This is most commonly in the context of compensatory mechanisms that reorganize the brain following in response to injury, disease or malformation, such as callosal agenesis (Tovar-Moll et al., 2014). Some of the most intriguing issues for scientific inquiries concern the manner and extent to which neuroplasticity occurs. A potential avenue for obtaining critical insights is to examine the nature of neuro-compensatory processes during human development when large structural abnormalities are present from birth.

The corpus callosum is the largest bundle of nerve fibers, estimated at 200 million, that enables direct communication between the two cerebral hemispheres

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of the brain, facilitating integration of motor, sensory, and cognitive processes (Paul et al., 2007; Taylor & David, 1998). Agenesis of the corpus callosum (AgCC) refers to a partial or complete absence of the corpus callosum since birth, with estimated prevalence varying somewhat across studies (1.8 per 10,000, including AgCC and hypoplasia, the latter referring to underdevelopment but not necessarily lack of the corpus callosum; Glass, Shaw, Ma, & Sherr, 2008). AgCC poses a broad range of deficits, often seen with associated anomalies and/or pervasive mental disorders and pronounced disabilities, including learning disorders and a high rate of epilepsy (Taylor & David, 1998). Curiously, however, some people with AgCC demonstrate subtle or almost unnoticeable symptoms. There are some very rare instances of individuals with complete callosal agenesis who are considerably high-functioning. These individuals strongly contrast with the numerous cases reported with more serious and often severe impairments (Bedeschi et al., 2006; Siffredi, Anderson, Leventer, & Spencer-Smith, 2013; Taylor & David, 1998). The underlying mechanisms leading to the range of severity and phenotypes are just beginning to be elucidated, with genetic advances providing key clues (see Paul et al., 2007 for a review). Evidence suggests polygenic and complex interactions are likely causes of AgCC phenotypes interrupting callosal development processes from neurogenesis to post-guidance development (Edwards, Sherr, Barkovich, & Richards, 2014; Paul et al., 2007). More importantly, reasons for a positive versus negative correlation of extent of agenesis and disabilities/impairments remain largely unknown. Furthermore, information is lacking as to how parents might be able to facilitate development in their child with AgCC and, in particular, foster appropriate and effective learning strategies and environments (Badaruddin et al., 2007).

The corpus callosum, widely studied in the context of surgical callosotomy to ameliorate symptoms of severe seizures in people with intractable epilepsy, is known to be critical in the normal coordination between the two hands (Bears, Connors, & Paradiso, 2007; Franz, 1997, 2003, 2012; Franz & Fahey, 2007; Franz & McCormick, 2010; Franz, Waldie, & Smith, 2000; Lassonde, Sauerwein, & Lepore, 2003), of which the manipulation and discrimination of objects is a primary example (Amazeen, Tseng, Valdez, & Vera, 2011; Dresslar, 1894; Flanagan & Bandomir, 2000; Lederman & Klatzky, 1993; Lehmann & Lampe, 1970). Callosal agenesis does not show the same disconnection syndrome as surgical disconnection and often reveals some evidence of interhemispheric transfer of information, which implicates forms of neuro-compensation (Tovar-Moll et al., 2014).

Many seemingly simple day-to-day tasks are achieved with minimal conscious effort to the complex interactions of our sensory, neural, and motor systems. Consider common manipulative tasks such as opening a bottle, lifting and placing objects, and picking fruits. Producing the appropriate and coordinated movements of the hands involved in such tasks requires an individual to have some idea of the weight and size of the objects. Such sensory-perceptual information is obtained through the dexterous movements of the motor systems involved (Amazeen, Tseng, Valdez, & Vera, 2011; Ellis & Lederman, 1993). Each hand's cutaneous mechanoreceptors respond to changing pressure sensed during object grasping (Goodwin & Wheat, 2008), and proprioceptive receptors respond to changes in muscle tension and length resulting from the forces required for lifting and moving objects (Giachritsis, Wright, & Wing, 2010; Halata & Baumann, 2008; Jones, 1986; Voisin, Lamarre, & Chapman, 2002). Afference from a single hand is projected to the contralateral cerebral cortex for interpretation or perception via the dorsal column-medial lemniscal pathway (cf. Figure 1) (Anton et al., 1996; Bears, Connors, & Paradiso, 2007; Fagot, Lacreuse, & Vauclair, 1997; Hsiao & Yau, 200`; Valdez & Amazeen, 2008). The corpus callosum comes into play particularly for the direct interhemispheric interactions involved in online cooperation between the hands (Franz, 2003, 2012) and in weight comparisons involving bimanual object manipulations (Bears, Connors, & Paradiso, 2007; Lassonde, Sauerwein, & Lepore, 2003). Furthermore, even though actions that are solely unimanual are thought to rely on predominantly contralateral projections, a small proportion (about 10-30%) of the descending tracts are thought to be non-crossed ipsilateral projections (Bears, Connors, & Paradiso, 2007; Ziemann et al., 1999), for which no functional role is so far known (cf. Figure 1).

A single study, conducted over four decades ago, investigated object weight discrimination in people with callosal agenesis, people with no neurological disorders (controls), and people with epilepsy (Lehmann & Lampe, 1970). In the most relevant experimental condition, participants were asked to hold a test weight in one hand while selecting a second object of equal weight using the other hand. Results revealed errors on the bimanual task that were nearly double in the acallosal group compared to the control group, both in terms of incorrect matches and in the estimated differences between test weights and selected weights (Lehmann & Lampe, 1970), which is suggestive of some disconnection syndrome. Since that study, almost 50 years have transpired, and no data has shown normal performance in people with

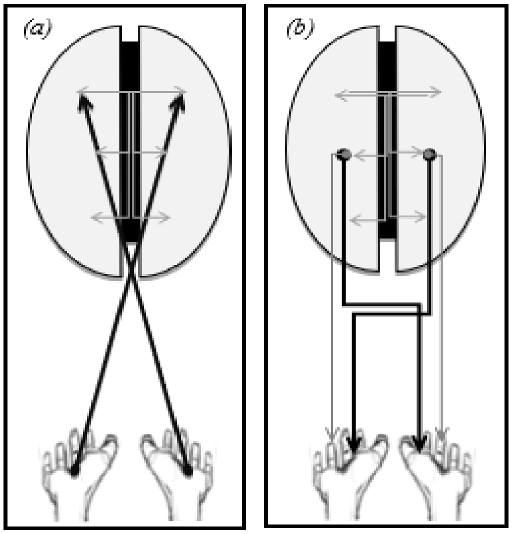

Figure 1. Schematic of input, output, and central cognitive comparator processes involved in weight discrimination. The intact corpus callosum is depicted as the black bar between hemispheres. Arrows indicate direction of information flow involving interhemispheric transfer of information. Panel (a) illustrates sensory pathways for weight perception from sensory receptors (cutaneous mechanoreceptors and proprioceptive receptors) to cortex. Panel (b) depicts motor pathways to hands for action generation and adjustment for contralateral (bold) and the ipsilateral (light) projections, the latter of which are believed to be of negligible functional contribution in the neurologically-normal brain.

callosal agenesis on such a dexterous task coordinating the two hands. Such a finding would encourage future-focused studies to identify forms of developmental neuro-compensation and neuroplasticity in addition to conditions (environmental, genetic, or a combination) that might promote optimal adaptations in behaviour. Therefore, tasks that have been established to rely on interhemispheric transfers, such as bimanual weight discrimination, and have shown a performance deficit in people with AgCC provide a powerful tool to interrogate the presence of possible neuro-compensatory mechanisms in high-functioning AgCC cases. Such tasks are useful because they rely on two elements of our ability to detect a true signal. This occurs when a stimulus is truly presented and someone recognizes the presence of the presented stimulus (a *hit*), as opposed to a *false* alarm when someone reports the presence of stimulus that is not truly there, or a *miss* when a stimulus is presented but not recognized. As such, in the Theory of Signal Detection, these tasks that capture both an individual's sensitivity to a target stimulus reflect the ability to detect or discriminate the target; *criterion* refers to a person's willingness to indicate the presence of the target stimulus (Allin, Matsuoka, & Klatzky, 2002; Danziger & Botwinick, 1980), or in the context of weight discrimination, one's own bias in judgment with respect to relevant factors.

The present study began with a simple question: is it possible for a high-functioning individual with complete absence of the primary connections between the two cerebral hemispheres to perform in the normal range on tasks that are known to rely heavily on the corpus callosum, such as precise weight comparisons of objects held in the two hands? Specifically, it was hypothesized that if a neuro-compensatory mechanism was present, then performance on a task reliant on the corpus callosum would fall within the normal range (± 2 standard deviations) of healthy controls, particularly for bimanual compared to unimanual comparisons. If so, such performance would be an initial step toward elucidating possible neuro-compensatory mechanisms.

Method

Participants

The family of a female with complete agenesis of the corpus callosum (16.5 years old during the present study) contacted our research team. The family and the patient (ACC1; described in detail below; cf. Figure 2) were keen to participate in research opportunities exploring AgCC. ACC1 is right-handed according to the *Edinburgh Handedness Inventory*, with a score of +100. Twenty female controls, in the 18-23 age range (M = 19.55, SD = 1.15), were recruited for a broader study on haptic weight discrimination, with an additional five female controls who were recruited and age-matched with ACC1. These five controls were between 16 and 17 years of age (M = 16.46, SD = 0.80). All controls (n = 30 in total) were recruited from the University of Otago community (New Zealand); all were strongly right-handed (M = 0.94: Oldfield, 1971), similar to ACC1. All participants were fully informed about the purpose of the study and were required to sign consent forms prior to testing. A parent or caretaker was asked to provide signed informed consent on behalf of those under the age of 18.

ACC1. Structural MRI scans (cf. Figure 2) revealed a clear absence of her entire corpus callosum. No other obvious abnormalities were present on radiological report other than apparent widened separation of lateral ventricles. No other sequences, such as diffusion-weighted imaging, were completed, as ACC1 did not want to continue the scanning due to the MRI scanner environment.

The following clinical observations and details were recorded during pre-testing interviews and are reported as such. Observations reported here were obtained from a neurologist report, interactions and

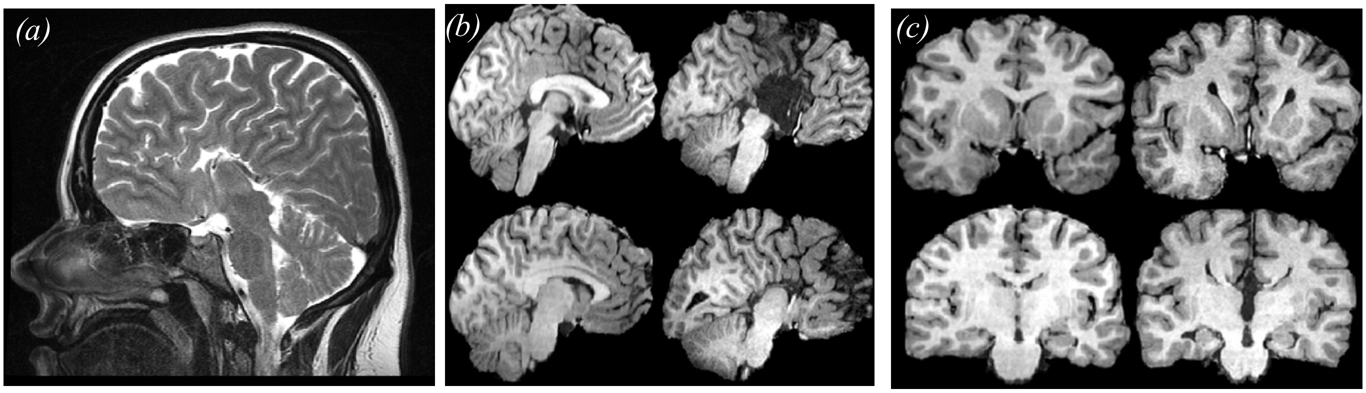

Figure 2. Structural MRI scans of ACC1 indicate complete agenesis of the corpus callosum in sagittal T2-weighted (panel (a)), T1-weighted sagittal (panel(b): right panel ACC1 in comparison to left panel depicting same-age neurologically-normal brain), and coronal (panel (c): right panel ACC1 in comparison to left panel depicting same-age neurologically-normal brain)

observations with ACC1 by the experimenters, and parent-reports.

Since AgCC is a rare disease and personal information about ACC1 is already provided (i.e. her age and the name of the establishment who recruited her), neuropsychological testing scores are not provided for confidentiality reasons. ACC1 was considered to be very high-functioning for someone diagnosed with AgCC, both by the experimenters and by the neurologist report. ACC1 had no hearing difficulties, no history of epilepsy, and has worn corrective lenses from a young age with the presence of *nystagmus* (involuntary eye movements). ACC1 attended regular secondary school. Her parents reported impressive skill levels in English, especially in reading and spelling, and in mathematics even though she had difficulties with algebra. ACC1 has excelled in more concrete subjects at school, but struggled a bit with more abstract concepts. Although she had difficulty in the past with fine motor unimanual skills like writing, she now demonstrates neat linked handwriting. She was also able to draw and copy drawings by others. ACC1 enjoyed textiles and sewing/crafts at school and has completed a kitchen skills achievement standard as part of a National Certificate of Educational Achievement in New Zealand. ACC1 texted on a cellphone using both hands and enjoyed computer games. However, she was quite sensitive to textured objects (particularly when she was younger) and was sometimes sensitive to loud noises. She was also known for staring at lights. As such, a screen for autism-related behaviours was conducted using the *Childhood Autism Rating Scale (second edition) High Functioning version* (CARS2-HF), which is more sensitive to detecting autistic features in verbally fluent individuals (Schopler, Van Bourgondien, Wellman, & Love, 2010). ACC1 scored in the *likely nonautistic* range with a very low level of autism-related symptoms compared to those with a diagnosis on the autism spectrum (total score = 26.5).

On the present task, ACC1 fully comprehended all instructions, was able to explain the instructions back to the experimenter, and even administered the instructions and the task to other members of her family. She was very attentive and certain of her answers when questioned further by the experimenter.

Apparatus

Twenty cylindrical plastic containers (height: 3.8 cm; lid diameter: 3.8 cm; base diameter: 3.5 cm; overall surface area: 63.94 cm^2) were filled with stones and fishing sinkers to produce hand-held weight stimuli ranging from 10 to 100 g at 5 g intervals (cf. Figure 3a). Two standard weights of 55 g were used as the midpoint of the stimulus series, which ranged from 45 g lighter than the standard (10 g weight), to 45 g heavier than the standard (100 g weight), with 19 pairs for comparison. Cotton wool packed in the containers prevented any noise cues. A blindfold was used to prevent any visual cues, thus ensuring discrimination via haptic and proprioceptive senses only.

Design and Procedure

Control participants were randomly assigned to one of two groups to make up a between-subjects factor of *instructions*. Group A were asked “are they the same?” and group B were asked “are they different?”, referring to two objects of comparison in each case. Participants in all conditions sat with their elbows and forearms resting on a table with hands positioned palms-up in a relaxed state. Small circles were drawn on the palms of the participants’ hands to guide the experimenter in placement of the stimulus. On each trial the experimenter placed the standard weight on the natural indent in the middle of one palm, as indicated by the circle. Prior to experimental trials, all

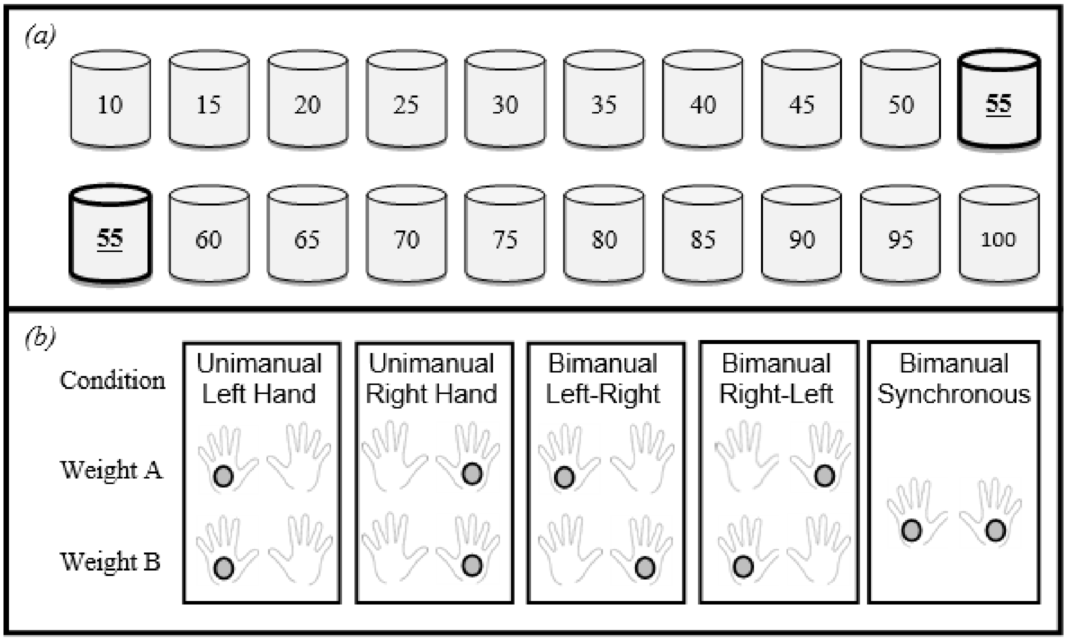

Figure 3. Weight stimuli and comparison conditions: a) weight stimuli used in the experiment ranging from 10 g to 100 g at 5 g intervals with two standard weights of 55 g; b) weight comparison conditions, showing the temporal sequence and hands used in each condition: weight A = time 1; weight B = time 2.

procedures were demonstrated and explained. The participant was encouraged to practice. This involved grasping the object placed on the palm by curving the fingers around it and then lifting it to the shoulder by bending at the elbow and then lowering the arm and releasing the weight, similar to techniques found in previous weight perception studies using neurologically-normal participants (Kahrimanovic, Bergmann Tiest, & Kappers, 2010).

Once it was clear that participants understood instructions, they were blindfolded. For each trial, the experimenter placed the required weight in the appropriate hand. The participant had 4 seconds to grasp, lift, and release the weight and then answer the question “are they the same?” (group A) or “are they different?” (group B). Scheduled breaks occurred between each condition or at a rate required by the participant to prevent fatigue.

The experiment with controls used a mixed-effects design with the between-subjects factor of instruction and two within-subject factors: 1) *weight difference* was measured in grams (g) from the standard at 5 g intervals and *2) weight presentation* had five different combinations. Each weight presentation condition measured participants’ ability to discriminate between the two weights (“are they the same?” or “are they different?”). There were two unimanual weight presentation conditions (left-hand unimanual and right -hand unimanual), which involved sequential placement of the first weight stimulus in one hand followed by the second weight stimulus to that same hand (cf. Figure 3b). There were also two temporally separated bimanual conditions (left-right bimanual and right-left bimanual) which also involved sequential placement with the first stimulus placed on the one hand and then, once released, the second stimulus placed on the other hand. The final condition was bimanual synchronous in which the two weights were simultaneously presented to the two hands and the grasping/lifting motions were to be made simultaneously.

Probabilities of stimulus presentation were controlled in an attempt to reduce response bias. Each condition had 96 trials in which 24 had two identical weights, 16 had two weights 5 g above or below the standard (a “close match”), and 56 had two weights that were 10-45 g above or below the standard. Furthermore, presentation of the standard occurred an equal number of times for each hand, with the first and second temporal order.

Each experimental session lasted approximately 90 minutes and consisted of 96 trials in randomized order for each of the five response conditions (also with randomized order). Participants returned one week later for a second session. In the second session, each participant repeated the above weight discrimination procedure with the five response conditions presented in a different order, so that no two sessions or participants were presented an identical order. ACC1 was tested on the same conditions with counterbalancing of instructions and weight presentation conditions across four sessions.

Data Reduction and Analysis

All analyses were conducted using Microsoft Excel 2010 and SPSS (version 18). Components of the Theory of Signal Detection were used to inform analysis, particularly the use of the discriminability index (*d'*) which measures the internal response to a stimulus independent of an individual's cognitive bias or response criterion (Stern & Johnson, 2010). To calculate *d*', the *hit rate* (proportion of *same* trials to which participants responded "same" for group A) and the *false alarm rate* (proportion of *different* trials to which participants responded "same" for group A) were calculated and transformed into *z*-scores where *d'* is equal to *z* (hit rate) – *z* (false alarm rate). The higher the value of *d'*, the greater the participant's ability to detect weight differences successfully, with a *d'* of zero representing chance (50%) (Heeger, 1998; Keating, 2005).

Each participant's responses from the two sessions were entered into an analysis in which the frequencies of "same" and "different" responses for each weight combination were calculated. The values were then averaged across positive and negative weight differences from the standard to obtain results for *absolute weight differences* (from the standard). For example, the 10 g and 100 g comparisons were combined to give the 45 g absolute difference from the standard. Following this, *d'* analyses were conducted on each individual's dataset.

For each of the two analysis, a mixed-effects ANOVA on the between-subject factor *instruction* (two-levels: "same" or "different") and the within-subject factor of *weight presentation* (five-levels: unimanual left, unimanual right, bimanual left-right, bimanual right-left, and bimanual synchronous) was conducted. We calculated effect size estimates for this model using eta squared (η^2) (Fritz, Morris, & Richler, 2012). Planned contrasts, corrected for multiple comparisons, were conducted to determine any differences between unimanual comparisons and bimanual comparisons.

Results

For the primary group of controls, a significant main effect of weight presentation for *d'* with a large effect size (Cohen, 1988) was found as shown in Figure 4, $F(4, 72) = 5.29$, $p = .018$, $\eta^2 = 0.22$, Greenhouse-Geisser corrected. The interaction between weight presentation and instruction was not significant, with a very small effect size $F(4, 72) = 1.29$, $p = .284$, $\eta^2 = 0.05$. Moreover, there was no significant differences between session one and session two for any of the response conditions ($p > .05$). Planned contrasts with corrections for multiple comparisons were conducted for all pairwise comparisons of the levels of weight presentations. All planned contrasts were significant, except those involving the unimanual left hand condition ($p < .05$), as seen in Figure 4. The best performance was observed in the unimanual right hand condition, whereas the lowest performance was observed for the bimanual left-right condition.

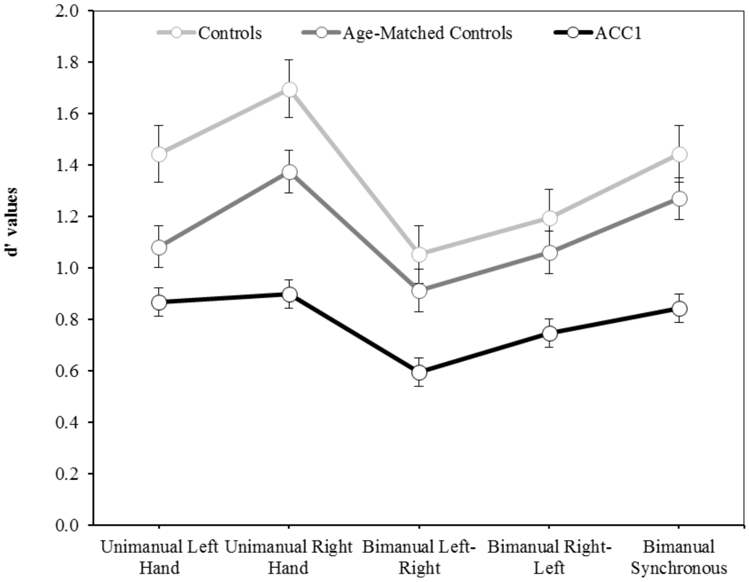

Figure 4. The mean *d'* values for neurologically-normal controls, the age-matched sample, and ACC1 across all weight presentation conditions. In each case, standard error is shown with bars.

The same pattern of results was found in the age-matched control sample (as seen in the primary group of controls; $p > .05$). With the performance of ACC1 being consistently well within 0.5-1.0 standard deviation of the primary control group, this suggests that age is not a limitation of the results. Specifically, as mentioned above, no significant differences were found between sessions ($p > .05$). It can be concluded that the ability to discriminate between two weights varies across response modality in neurologically-healthy controls.

Using the same data reduction and analysis for ACC1, her *d'* analysis revealed performance clearly above chance levels in all conditions, with a pattern of performance across conditions similar to that of controls (including the age-matched sample) (cf. Figure 4). The *d'* scores of ACC1 are within 1 standard deviation of the distribution of control data in the unimanual right hand condition and well within 1-2 standard deviations in all other conditions (cf. Table 1).

These data revealed that ACC1 performed above chance levels at weight discrimination and followed the same trend as controls. Her performance cannot be clearly discriminated from the control groups. Therefore, it appears she is not clearly disadvantaged in simple bimanual comparisons, as one might have expected given the lack of a corpus callosum.

Discussion

Using a systematic design to determine humans' ability to haptically discriminate weights, this study examined if between-hemisphere weight comparisons (bimanual) would yield poorer weight discrimination (i.e., lower *d'* values), particularly in a person without a corpus callosum. Overall, findings suggest that synchronous bimanual haptic weight discrimination is performed as well as unimanual weight discrimination, when taking both unimanual conditions into account; although both bimanual synchronous and the unimanual response modalities produced superior performance to the sequential bimanual response modality. Most importantly, the pattern of results was very similar across the control groups and ACC1, and a very similar pattern of effects across conditions were found for the two instructional modalities (whether making decisions that two weights were the same or different), further indicating that the form of question used did not significantly influence decisional processes. ACC1 was well within 1-2 standard deviations of the control distribution on all conditions, revealing performance that cannot be clearly distinguished from that of people with an intact corpus callosum. To summarize these primary results, ACC1 was clearly capable of discriminating weights using haptic judgments, demonstrating this ability across both unimanual and bimanual presentation modalities.

Below, results are discussed in terms of their implications on high-order processes in the neurological normal brain. This work highlights how remarkable the human brain can be. Even when the corpus callosum is congenitally absent, functions as important as weight discrimination can still be performed with a high level of competence. In turn, this suggests the presence of possible mechanisms to explain the observed performance of ACC1 (cf. Figure 5, top panel) relative to controls (cf. Figure 5, bottom panel).

The primary finding of interest is that both hemispheres of the brain can ostensibly process weight and discriminate between same and different weights reasonably well, a finding that has not been shown in the literature before to our knowledge. Moreover, within the bimanual sequential comparisons, *d*' was consistently at its lowest when the left hand preceded the right hand in holding of the weights, for both controls and ACC1. This finding suggests support for the notion of left hemisphere (right hand) dominance (which is consistent with being right-handed; Oldfield, 1971). Of potential relevance, it is noted that the right hand on its own appears to be more sensitive to the discrimination of two weights (and all participants were strongly right-handed), which raises two key possibilities. Perhaps the right hand is superior at weight discrimination

Table 1

Control sample distribution mean (top row), mean of ACC1 (middle row), and Standard Deviation of ACC1 from the Mean Weight Discrimination (d') of Neurologically-Normal Control Participants (bottom row) for the different experimental conditions.

	Unimanual Left Hand	Unimanual Right Hand	Bimanual Left-Right	Bimanual Right-Left	Bimanual Synchronous
Control mean ($n = 20$)	1.440	1.700	1.050	1.190	1.440
ACC1 mean	0.868	0.897	0.593	0.763	0.827
Standard deviation of ACC1's scores relative to control distribution	1.679	0.706	1.510	1.354	1.254

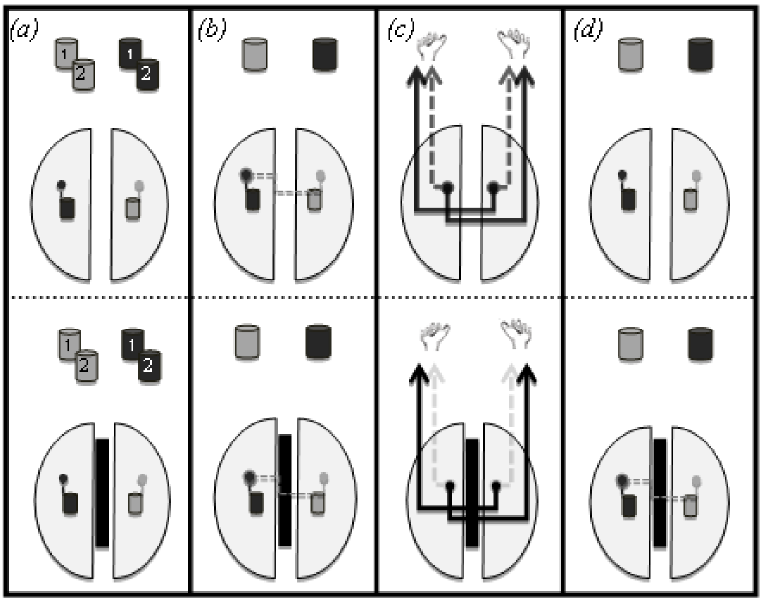

Figure 5. Possible models for weight comparisons in ACC1 (top panel) and neurologically-normal controls (lower panel) with intact corpus callosi (depicted as a black bar): Model one (panel (a)): Unimanual weight comparisons processed by the hemisphere contralateral to the stimulated hand do not require callosal interactions for successful discrimination, thereby predicting identical effects in ACC1 and controls; Model two (panel (b)); Weight comparisons may occur via a subcortical pathway in ACC1 and in controls, and this compensates for the lack of callosal fibers in ACC1 (dotted lines in each case represent subcortical transfer), also predicting similar effects in ACC1 and controls; Model three (panel (c)): Bimanual weight comparisons via stronger ipsilateral projections in ACC1 compared to controls. Contralateral output projections are shown in bold with the assumed known dominance of approximately 80% crossed; extra ipsilateral projections are shown as dashed lines, which are bolder in ACC1 (top panel). Predictions differ for ACC1 and controls, although one must consider possible callosal interactions in the controls that would not assist ACC1, although the interplay of ipsilateral projections and callosal processes is not yet known and would have to be further disentangled, and Model four (panel (d)): Inability in ACC1 to communicate information from one hemisphere to another leading to chance performance, in contrast to controls who would perform better due to callosal transfer of information.

because it was the dominant hand in all participants. For example, it may be more sensitive due to increased use in everyday life including sensory discrimination such as weight. Alternatively, the right hand may be more able to discriminate weights because the left hemisphere of the brain may be superior to the right hemisphere at haptic processing and/or weight discrimination, as has been debated in the literature (Fagot, Lacreuse, & Vauclair, 1997; Kaas, Stoeckel, & Goebel, 2008; Nishizawa, 1991). It is also of interest that left hand unimanual performance was equal to the bimanual-synchronous condition, which suggests that the left hand may be a limiting factor in bimanual processing of weights for haptic discrimination. The *limiting effect* is a possibility as there were no additive effects seen in the neurologically-healthy controls to suggest enhancement of discriminability when using both hands in synchrony or in sequence. Future research with left-handed individuals would be beneficial to clarify these observations and the interpretation of findings.

The decreased sensitivity in bimanual sequential compared to unimanual sequential conditions may be a result of the memory processes involved when there is a delay in presentation, as synchronous weight presentation bimanually does not decrease sensitivity as significantly. This may result from the memory process involved in maintaining the information from weight A (cf. Figure 5b) for comparison with weight B which would require both hemispheres in bimanual conditions, thereby contributing to cognitive load which could diminish performance. Future research should include neuropsychological testing, particularly for intelligence quotient (IQ), memory, attention, and sensory processing, to unpack the potential contribution of these processes to a neuro-compensatory mechanism. The finding that *d'* was consistently at its lowest for both controls and ACC1 when the left hand preceded the right hand in holding of the weights is also consistent with the notion of left hemisphere (right hand) dominance. This would also be consistent with the possibility that the left hemisphere projects fibers to the right hemisphere to inhibit it during development (Corballis & Morgan, 1978). Therefore, it is plausible that the left hemisphere is favored in the transfer of information which results in better performance when the left hemisphere is dominant in sequential bimanual comparisons of weight (i.e., when the right hand leads the comparative sequence). These are all issues requiring further research.

As already emphasized, ACC1's performance indicates a substantially above chance ability to discriminate weights successfully in both unimanual and in all bimanual discrimination conditions tested. Strikingly, ACC1's performance relative to controls reveals the same basic pattern, with her performance never falling below two standard deviations of the mean of controls. These results support the possibility of a subcortical comparative mechanism being used by ACC1 to compare weights bimanually (cf. Figure 5b). If a subcortical mechanism were involved, this process would most likely be slower and potentially less accurate in transferring information, thereby accounting for the slight decrease in sensitivity to weight differences in the data of ACC1 compared to controls. It is debatable, however, whether the four seconds response window used in the present study is still ample time to allow for the transmission of information, even at decreased rates, and may represents a limitation of the current study to external validity. To ensure some experimental control over timing, the four-second timing was used. Of note, the present task using real objects poses constraints on trial time because the task requires far more time than estimates of callosal transfer even with an intact callosum. Any decrease in sensitivity via such a subcortical pathway could be due to the length of the pathway or the nature of the pathway. For example, it may be that a compensatory pathway developed for general communication rather than as a specialized mechanism for certain types of information (as in the case of the corpus callosum). The current study is limited in its ability to distinguish between possible compensatory mechanisms, and further research is required to disentangle and understand the mechanisms underpinning this phenomenon through behavioural and neuroimaging work.

A second model, that of the presence of active ipsilateral projections, may account for ACC1's ability to discriminate weights in the bimanual conditions. An important source of information in the discrimination of weights comes from motor output and feedback projections. To gain sensory information an action must be generated—the initial action is then corrected with sensory information to obtain the right force and tension to lift the object. This corrective process is posited as being very influential in the judgment of weight. In neurologically—normal individuals, the motor output projections are predominantly contralateral (approximately 80%). However, studies have shown that in callosal agenesis, there can be a strengthening of ipsilateral projections that may aid in the ability to coordinate bimanual functions (Ziemann et al., 1999). Accordingly, it is possible that in ACC1, the motor information from the right hand is projected to the contralateral hemisphere (left hemisphere) and also to the ipsilateral hemisphere (right hemisphere). Likewise, information from the left hand might be projected to both the right hemisphere (contralateral) and left hemisphere (ipsilateral) (cf. Figure 5c). As a result, the comparison could occur in one hemisphere only as information from each hand would be present; if ipsilateral tracts were indeed enlarged in ACC1, then the ipsilateral information might be strong enough for a comparison of weights at an above chance level as seen in this study.

The ability of ACC1 to perform successful weight comparisons bimanually likely points to the remarkable compensatory ability of the human brain. People with callosal agenesis tend not to display the classic "disconnection syndrome" of callosotomy and commissurotomy patients. Some of the most famous findings of the "disconnection syndrome", such as difficulties naming or describing material presented to the left visual field, are not seen in identical tests performed by people with callosal agenesis (Sperry, 1970), nor are they seen as remarkably in ACC1. As a result, it is highly likely that this difference reveals effects of plasticity in the brain and central nervous system. Our earlier work with three participants with callosal agenesis revealed a lack of rudimentary callosal interactions on a simple bimanual response task (Franz & Fahey, 2007). One of the participants tested in that study was ACC1. Thus, without such rudimentary callosal interactions, it is likely that forms of developmental plasticity compensate for a lack of communication between the cerebral hemispheres. This might include the strengthening of ipsilateral projections and/or subcortical structures to allow for integration of information between the two hemispheres, as described above (Chiarello, 1980; Lassonde, Sauerwein, Chicoine, & Geoffroy, 1991).

The results of this study indicate there may be a neuro-compensatory mechanism present in ACC1, facilitating her ability to perform a task known to rely on the corpus callosum. This has implications for the clinical evaluation of AgCC, where standard tests of behaviour and cognition may not readily identify AgCC without neuroimaging, but rather present a mixed profile or subtle performance deficits. Practitioners should aim to identify an individual's neuro-compensatory mechanism so they can be best supported through assessment and treatment strategies that harness this mechanism. While the precise mechanism is unable to be identified, this suggests that there is potential benefit in clinical and learning strategies that promote interhemispheric communication. Similarly, cross-hemisphere cognitive strategies may support development of, or strengthen, neuro-compensatory mechanisms in children with AgCC. These may include cognitive exercises, such as memory and attention, or sensory-motor exercises, such as tasks relying on coordination or development of more granular sensory-motor networks.

It is plausible that if the corpus callosum does not begin to form as in typical neurodevelopment, opportunities arise for other pathways that naturally exist in the young brain and central nervous system. These pathways may have unrestrained development without the competing (and dominant) development of such a significant interhemispheric band of fibers. Of note, however, not all people with callosal agenesis are as high-functioning as ACC1 or the others in our earlier study (Franz & Fahey, 2007). In fact, it has been noticed across testing with people who have various degrees of callosal agenesis, that those with complete agenesis (as in ACC1) tend to be far more highly functioning than those with partial agenesis (though this inference comes from our own limited sample).

Conclusion

Neurologically-normal controls are able to discriminate weight differences reasonably well using haptic information and no vision. The results of ACC1 clearly indicate that weight discrimination is possible at well above chance levels, both unimanually and bimanually. A parsimonious interpretation is that this provides novel evidence for an alternative mechanism to the corpus callosum, which allows for comparative judgments of weights between the two hands (although there are other possibilities, as detailed above). This key finding may reflect plasticity of the brain and central nervous system in callosal agenesis via a subcortical hemispheric communication mechanism, and/or strengthening of ipsilateral motor projections.

It is important that clinicians and researchers take the opportunity to learn from naturally-occurring anomalies, as we are constantly reminded that ACC1 demonstrates a remarkable example of the human ability to adapt. People with a normal corpus callosum rely on that structure for their everyday activities, such as buttoning, texting, tying shoelaces, and opening jars, to mention a few among a vast range of bimanual activities. Here, we have a remarkable example of a young woman who cannot rely on this brain structure to perform such tasks, yet she is still able to integrate information and adapt in a manner that reveals within normal ranges of performance. People such as ACC1 offer such valuable examples of what human beings are capable of, and they make such important and valuable contributions to society if given the opportunity to learn and adapt and thus to reach their potential. They may lack their corpus callosum, but this should not be taken to mean that they lack the integrative skills to function successfully in their lifetime.

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